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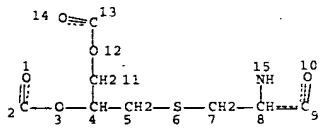
=> d his nofile l1-17; d que stat l8; d his nofile l9-

     (FILE 'HOME' ENTERED AT 13:31:21 ON 20 SEP 2007)

     FILE 'LREGISTRY' ENTERED AT 13:31:27 ON 20 SEP 2007
L1                STR
L2              0 SEA SSS SAM L1
L3                STR L1

     FILE 'REGISTRY' ENTERED AT 13:36:42 ON 20 SEP 2007
L4              0 SEA SSS SAM L1
L5                STR L1
L6             46 SEA SSS SAM L5
L7              0 SEA ABB=ON  PLU=ON  L6 AND C2H4O


L5                STR
```



← Covers claim 1,5,6,7,12,13

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  15

STEREO ATTRIBUTES: NONE
L8            934 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED    2755 ITERATIONS                 934 ANSWERS
SEARCH TIME: 00.00.01



     (FILE 'REGISTRY' ENTERED AT 13:36:42 ON 20 SEP 2007)
                SAVE L8 TEMP HA013STR/A
L9             14 SEA ABB=ON  PLU=ON  L8 AND C2H4O


     FILE 'REGISTRY' ENTERED AT 13:40:01 ON 20 SEP 2007
L10            14 SEA ABB=ON  PLU=ON  L8 AND PMS/CI
L11            14 SEA ABB=ON  PLU=ON  L10 OR L9

     FILE 'CAPLUS' ENTERED AT 13:41:06 ON 20 SEP 2007
L12             7 SEA ABB=ON  PLU=ON  L11
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L13             0 SEA ABB=ON  PLU=ON  L11

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L14            19 SEA ABB=ON  PLU=ON  MUHLRADT P?/AU
L15            91 SEA ABB=ON  PLU=ON  MORR M?/AU
L16           106 SEA ABB=ON  PLU=ON  (L14 OR L15)
L17             1 SEA ABB=ON  PLU=ON  L16 AND L12
L18         89063 SEA ABB=ON  PLU=ON  MACROPHAG?/OBI
L19        203010 SEA ABB=ON  PLU=ON  DRUG DELIV?/OBI
L20        223433 SEA ABB=ON  PLU=ON  ANTITUMO?/OBI OR ANTI INFECTIV?/OBI
L21        209990 SEA ABB=ON  PLU=ON  WOUND/OBI OR HEAL?/OBI OR IMMUNOSTIM?/OBI
L22        670702 SEA ABB=ON  PLU=ON  (L18 OR L19 OR L20 OR L21)
L23            24 SEA ABB=ON  PLU=ON  L16 AND L22
L24            24 SEA ABB=ON  PLU=ON  L23 OR L17
L25            23 SEA ABB=ON  PLU=ON  L24 NOT L12

     FILE 'REGISTRY' ENTERED AT 13:47:24 ON 20 SEP 2007
                E 52-90-4
L26             1 SEA ABB=ON  PLU=ON  52-90-4
                D SCAN

     FILE 'CAPLUS' ENTERED AT 13:47:44 ON 20 SEP 2007
L27          1916 SEA ABB=ON  PLU=ON  L26/D
L28           247 SEA ABB=ON  PLU=ON  BISACYL?/OBI
L29        292351 SEA ABB=ON  PLU=ON  POLYETHYLENE/OBI
L30        305399 SEA ABB=ON  PLU=ON  PEG/OBI OR L29
L31        305642 SEA ABB=ON  PLU=ON  L28 OR L30
L32            55 SEA ABB=ON  PLU=ON  L27 AND L31
L33            10 SEA ABB=ON  PLU=ON  L27 (L) L31
L34             9 SEA ABB=ON  PLU=ON  L33 NOT (L12 OR L25)
                D QUE STAT L8

=> fil reg
FILE 'REGISTRY' ENTERED AT 13:50:57 ON 20 SEP 2007
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STRUCTURE FILE UPDATES:   19 SEP 2007  HIGHEST RN 947584-60-3
DICTIONARY FILE UPDATES:  19 SEP 2007  HIGHEST RN 947584-60-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> d que sta l8
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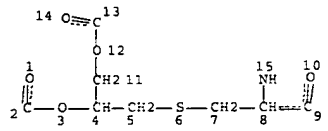
L5 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 2755 ITERATIONS 934 ANSWERS
SEARCH TIME: 00.00.01

=> d que stat l11
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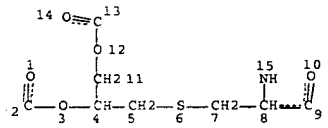

← covers claims 1,5,6,7,12,13

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L8 934 SEA FILE=REGISTRY SSS FUL L5
L9 14 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND C2H4O
L10 14 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND PMS/CI
L11 14 SEA FILE=REGISTRY ABB=ON PLU=ON L10 OR L9

=> fil caplus
FILE 'CAPLUS' ENTERED AT 13:51:22 ON 20 SEP 2007
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FILE COVERS 1907 - 20 Sep 2007 VOL 147 ISS 13
FILE LAST UPDATED: 19 Sep 2007 (20070919/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> fil reg
FILE 'REGISTRY' ENTERED AT 13:51:59 ON 20 SEP 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES: 19 SEP 2007 HIGHEST RN 947584-60-3
DICTIONARY FILE UPDATES: 19 SEP 2007 HIGHEST RN 947584-60-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

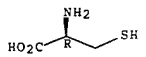
http://www.cas.org/support/stngen/stndoc/properties.html

=> d que 126; d l26
L26 1 SEA FILE=REGISTRY ABB=ON PLU=ON 52-90-4

L26 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 52-90-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Cysteine (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cysteine, L- (8CI)
OTHER NAMES:

CN (R)-2-Amino-3-mercaptopropanoic acid
CN (R)-Cysteine
CN β-Mercaptoalanine
CN 2-Amino-3-mercaptopropionic acid
CN Cystein
CN Cysteine
CN E 920
CN Half-cystine
CN L-(+)-Cysteine
CN L-Alanine, 3-mercapto-
CN L-Cys
CN NSC 8746
CN Propanoic acid, 2-amino-3-mercapto-, (R)-
CN Thioserine
FS STEREOSEARCH
DR 4371-52-2
MF C3 H7 N O2 S
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, USPATOLD, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

41899 REFERENCES IN FILE CA (1907 TO DATE)
1907 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
42027 REFERENCES IN FILE CAPLUS (1907 TO DATE)
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> fil caplus
FILE 'CAPLUS' ENTERED AT 13:52:12 ON 20 SEP 2007
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FILE COVERS 1907 - 20 Sep 2007 VOL 147 ISS 13
FILE LAST UPDATED: 19 Sep 2007 (20070919/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos 112
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L9 14 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND C2H4O
L10 14 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND PMS/CI
L11 14 SEA FILE=REGISTRY ABB=ON PLU=ON L10 OR L9
L12 7 SEA FILE=CAPLUS ABB=ON PLU=ON L11 ← structure search

=> d que nos 125
L5 STR
L8 934 SEA FILE=REGISTRY SSS FUL L5
L9 14 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND C2H4O
L10 14 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND PMS/CI
L11 14 SEA FILE=REGISTRY ABB=ON PLU=ON L10 OR L9
L12 7 SEA FILE=CAPLUS ABB=ON PLU=ON L11
L14 19 SEA FILE=CAPLUS ABB=ON PLU=ON MUHLRADT P?/AU
L15 91 SEA FILE=CAPLUS ABB=ON PLU=ON MORR M?/AU
L16 106 SEA FILE=CAPLUS ABB=ON PLU=ON (L14 OR L15)
L17 1 SEA FILE=CAPLUS ABB=ON PLU=ON L16 AND L12
L18 89063 SEA FILE=CAPLUS ABB=ON PLU=ON MACROPHAG?/OBI
L19 203010 SEA FILE=CAPLUS ABB=ON PLU=ON DRUG DELIV?/OBI
L20 223433 SEA FILE=CAPLUS ABB=ON PLU=ON ANTITUMO?/OBI OR ANTI INFECTIV?/OBI
L21 209990 SEA FILE=CAPLUS ABB=ON PLU=ON WOUND/OBI OR HEAL?/OBI OR IMMUNOSTIM?/OBI
L22 670702 SEA FILE=CAPLUS ABB=ON PLU=ON (L18 OR L19 OR L20 OR L21)
L23 24 SEA FILE=CAPLUS ABB=ON PLU=ON L16 AND L22
L24 24 SEA FILE=CAPLUS ABB=ON PLU=ON L23 OR L17
L25 23 SEA FILE=CAPLUS ABB=ON PLU=ON L24 NOT L12 ← inventor search

=> d que nos 134
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L10 14 SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND PMS/CI
L11 14 SEA FILE=REGISTRY ABB=ON PLU=ON L10 OR L9
L12 7 SEA FILE=CAPLUS ABB=ON PLU=ON L11
L14 19 SEA FILE=CAPLUS ABB=ON PLU=ON MUHLRADT P?/AU
L15 91 SEA FILE=CAPLUS ABB=ON PLU=ON MORR M?/AU
L16 106 SEA FILE=CAPLUS ABB=ON PLU=ON (L14 OR L15)
L17 1 SEA FILE=CAPLUS ABB=ON PLU=ON L16 AND L12
L18 89063 SEA FILE=CAPLUS ABB=ON PLU=ON MACROPHAG?/OBI
L19 203010 SEA FILE=CAPLUS ABB=ON PLU=ON DRUG DELIV?/OBI
L20 223433 SEA FILE=CAPLUS ABB=ON PLU=ON ANTITUMO?/OBI OR ANTI INFECTIV?/OBI
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              IMMUNOSTIM?/OBI
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L24           24 SEA FILE=CAPLUS ABB=ON  PLU=ON  L23 OR L17
L25           23 SEA FILE=CAPLUS ABB=ON  PLU=ON  L24 NOT L12
L26            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  52-90-4
L27         1916 SEA FILE=CAPLUS ABB=ON  PLU=ON  L26/D
L28          247 SEA FILE=CAPLUS ABB=ON  PLU=ON  BISACYL?/OBI
L29       292351 SEA FILE=CAPLUS ABB=ON  PLU=ON  POLYETHYLENE/OBI
L30       305399 SEA FILE=CAPLUS ABB=ON  PLU=ON  PEG/OBI OR L29
L31       305642 SEA FILE=CAPLUS ABB=ON  PLU=ON  L28 OR L30
L33           10 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 (L) L31
L34            9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 NOT (L12 OR L25)
```

← derivatives cycteine

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=> d .ca hitstr l12 1-7;d .ca l25 1-23; d .ca l34 1-9

L12  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:818137  CAPLUS  Full-text
DOCUMENT NUMBER:          145:209272
TITLE:                    Lipid carriers for lymphocyte epitopes
INVENTOR(S):              Jackson, David C.; Zeng, Weiguang
PATENT ASSIGNEE(S):       The Council of the Queensland Institute of Medical
                          Research, Australia
SOURCE:                   PCT Int. Appl., 98pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.            KIND   DATE         APPLICATION NO.          DATE
     ----------------      ----   --------     -------------------      --------
     WO 2006084319          A1    20060817     WO 2006-AU162            20060208
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                        AU 2005-900571      A  20050208
OTHER SOURCE(S):          MARPAT 145:209272
ED   Entered STN:  17 Aug 2006
AB   The authors disclose immunogenic mols. capable of stimulating an immune
     response to peptide epitopes irresp. of the HLA type.  In one example, the
     immunostimulatory carrier comprises a peptide derivative of dipalmitoyl-S-
     glyceryl cysteine (Pam2Cys).
CC   15-2 (Immunochemistry)
IT   904925-17-3D, conjugates with immunogens  904925-18-4D, conjugates with
     immunogens  904925-19-5D, conjugates with immunogens  904925-20-8D,
     conjugates with immunogens 904925-21-9D, conjugates with
     immunogens 904925-22-0D, conjugates with immunogens
     904925-23-1D, conjugates with immunogens 904925-24-2D,
     conjugates with immunogens
```



```
     RL: BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (enhanced immune response to)
IT   904925-21-9D, conjugates with immunogens 904925-22-0D,
     conjugates with immunogens 904925-23-1D, conjugates with
     immunogens 904925-24-2D, conjugates with immunogens
     RL: BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (enhanced immune response to)
RN   904925-21-9  CAPLUS
CN   Poly(oxy-1,2-ethanediyl), α-[3-[[(1R)-2-amino-1-(mercaptomethyl)-2-
     oxoethyl]amino]-3-oxopropyl]-ω-hydroxy-, 3-ether with
     S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-L-cysteinyl-L-seryl-N-(2-
     hydroxyethyl)-L-serinamide (9CI)  (CA INDEX NAME)
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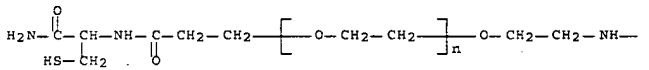
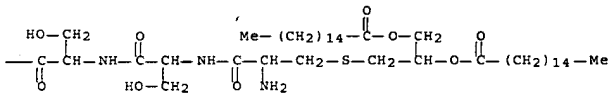
PAGE 1-A



PAGE 1-B



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RN   904925-22-0  CAPLUS
CN   Poly(oxy-1,2-ethanediyl), α-[3-[[(1R)-2-amino-1-(mercaptomethyl)-2-
     oxoethyl]amino]-3-oxopropyl]-ω-hydroxy-, 4-ether with
     N2,N6-bis[S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-L-cysteinyl]-L-lysyl-L-
     seryl-N-(2-hydroxyethyl)-L-serinamide (9CI)  (CA INDEX NAME)
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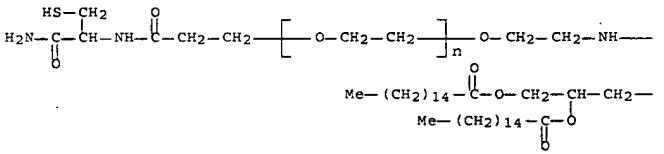
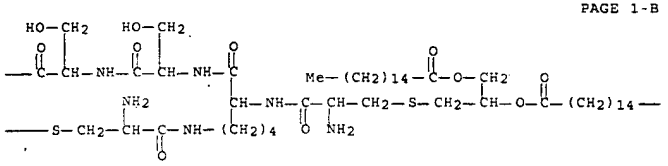
PAGE 1-A



PAGE 1-B



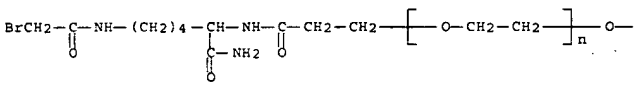
PAGE 1-C

—Me

RN 904925-23-1 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[3-[[(1S)-1-(aminocarbonyl)-5-[(bromoacetyl)amino]pentyl]amino]-3-oxopropyl]-ω-hydroxy-, 3-ether with S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-L-cysteinyl-L-seryl-N-(2-hydroxyethyl)-L-serinamide (9CI) (CA INDEX NAME)

PAGE 1-A



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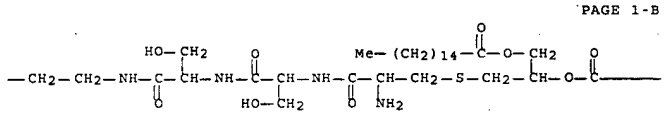


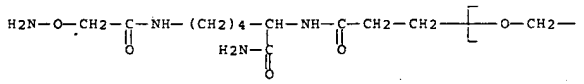
PAGE 1-C

—(CH2)14—Me

RN 904925-24-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[3-[[(1S)-1-(aminocarbonyl)-5-[[(aminooxy)acetyl]amino]pentyl]amino]-3-oxopropyl]-ω-hydroxy-, 3-ether with S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-L-cysteinyl-L-seryl-N-(2-hydroxyethyl)-L-serinamide (9CI) (CA INDEX NAME)

PAGE 1-A



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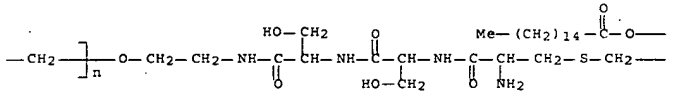
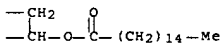


PAGE 1-C



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:796105 CAPLUS Full-text
DOCUMENT NUMBER: 145:229322
TITLE: Lipid-based adjuvants targeting dendritic cells
INVENTOR(S): Jackson, David C.; Parish, Christopher Richard
PATENT ASSIGNEE(S): Lipotek Pty Ltd, Australia
SOURCE: PCT Int. Appl., 25pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006081631	A1	20060810	WO 2006-AU147	20060207
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006209809	A1	20060810	AU 2006-209809	20060207
PRIORITY APPLN. INFO.:			AU 2005-900518 A	20050207
			WO 2006-AU147 W	20060207

ED Entered STN: 11 Aug 2006

AB The authors disclose the preparation and immunostimulatory activity of adjuvants comprising a lipid-based dendritic cell targeting moiety covalently linked to a metal chelating group. Further, the authors disclose immunogens comprising (a) a lipid-based dendritic cell targeting moiety covalently linked to a metal chelating group; (b) an antigen comprising a metal affinity tag, and optionally (c) metal ions, whereby the antigen is linked to the lipid-based dendritic cell targeting moiety via the interaction between the metal affinity tag and the metal chelating group.

CC 15-2 (Immunochemistry)
Section cross-reference(s): 2, 34

IT 139-13-9D, Nitrilotriacetic acid, palmitoylcysteine derivs. 905312-92-7D, nitrilotriacetic/succinimidyl maleimidocaproate derivs., chelate with hexahistidine-tagged antigens 905312-93-8D, chelate with hexahistidine-tagged antigens
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(adjuvant activity of)

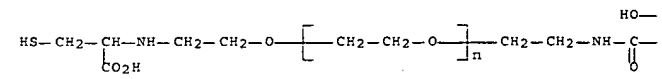
IT 905312-90-5P 905312-91-6P 905312-92-7P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(lipid moiety of synthetic adjuvant targeting dendritic cells)

IT 905312-92-7D, nitrilotriacetic/succinimidyl maleimidocaproate derivs., chelate with hexahistidine-tagged antigens
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(adjuvant activity of)

RN 905312-92-7 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[2-[[(1R)-1-carboxy-2-mercaptoethyl]amino]ethoxy]-ω-hydroxy-, 31-ether with S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-L-cysteinyl-L-seryl-N-(2-hydroxyethyl)-L-serinamide (9CI) (CA INDEX NAME)

PAGE 1-A



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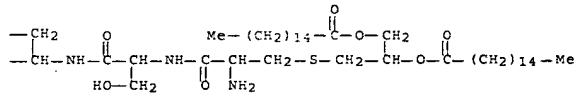


RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(lipid moiety of synthetic adjuvant targeting dendritic cells

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

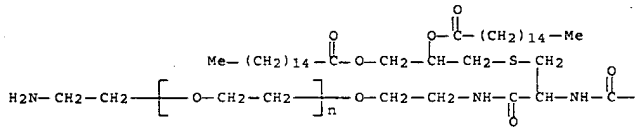
L12 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:55397 CAPLUS Full-text
DOCUMENT NUMBER: 140:105268
TITLE: Macrophage-stimulating bisacyloxypropylcysteine conjugates and therapeutic use thereof
INVENTOR(S): Muehlradt, Peter F.; Morr, Michael
PATENT ASSIGNEE(S): GBF Gesellschaft fuer Biotechnologische Forschung MbH, Germany
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1382352	A1	20040121	EP 2002-16066	20020719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2489010	A1	20040129	CA 2003-2489010	20030718
WO 2004009125	A2	20040129	WO 2003-EP7892	20030718
WO 2004009125	A3	20040527		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003251002	A1	20040209	AU 2003-251002	20030718

EP 1521600 A2 20050413 EP 2003-765055 20030718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2006134061 A1 20060622 US 2005-521013 20050913
PRIORITY APPLN. INFO.: EP 2002-16066 A 20020719
WO 2003-EP7892 W 20030718

OTHER SOURCE(S): MARPAT 140:105268
ED Entered STN: 22 Jan 2004
AB The invention discloses bisacyloxypropylcysteine conjugates R2C(O)OCH[R1C(O)OCH2]CH2SCH(NH2)C(O)YR3 (R1, R2 = fatty acid group; Y = NH, O, S, OCO; R3 = conjugate group, especially a polymer). Conjugates of the invention include e.g. S-[2,3-bis(palmitoyloxy)-(2S)-propyl]-L-cysteinyl-carboxy-polyethylene glycol. The conjugates of the invention show good macrophage-stimulating activity and need no other solubilizers. They are useful for numerous applications, particularly for macrophage stimulation, stimulation of antibody production, as a defense against infection, as immunostimulants, particularly in relation to tumors, for the prevention and treatment of septic shock, for wound healing, and as adjuvants for vaccines.
IC ICM A61K047-48
CC 1-7 (Pharmacology)
Section cross-reference(s): 34
IT 647013-57-8
RL: PAC (Pharmacological activity); BIOL (Biological study)
(macrophage-stimulating bisacyloxypropylcysteine conjugates and therapeutic use)
IT 647013-56-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrophage-stimulating bisacyloxypropylcysteine conjugates and therapeutic use)
IT 647013-57-8
RL: PAC (Pharmacological activity); BIOL (Biological study)
(macrophage-stimulating bisacyloxypropylcysteine conjugates and therapeutic use)
RN 647013-57-8 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(2-aminoethyl)-ω-[2-[[(2R)-3-[[(2S)-2,3-bis[(1-oxohexadecyl)oxy]propyl]thio]-1-oxo-2-[(1-oxohexadecyl)amino]propyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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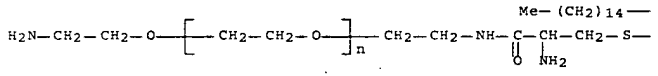
IT 647013-56-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrophage-stimulating bisacyloxypropylcysteine conjugates and therapeutic use)
RN 647013-56-7 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[[(2R)-2-amino-3-[[(2S)-2,3-bis[(1-oxohexadecyl)oxy]propyl]thio]-1-oxopropyl]amino]ethyl]-ω-(2-aminoethoxy)- (9CI) (CA INDEX NAME)

PAGE 1-A



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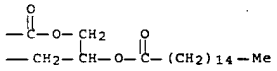
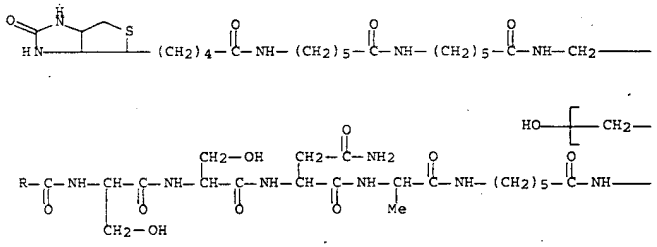


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:639679 CAPLUS Full-text
DOCUMENT NUMBER: 125:295931
TITLE: Biotin, consensus sequence, lipoamino acid and the antigenic Dnp-group combine to a synthetic substrate for enzymes involved in lipoprotein biosynthesis
AUTHOR(S): Feiertag, S.; Wiesmueller, K. -H.; Metzger, J. W.; Schnerring, K.; Goetz, F.; Jung, G.
CORPORATE SOURCE: Naturwissenschaftliches und Medizinisches Institut, Universitat Tubingen, Reutlingen, D-72762, Germany
SOURCE: Peptides 1994, Proceedings of the European Peptide Symposium, 23rd, Braga, Port., Sept. 4-10, 1994 (1995), Meeting Date 1994, 895-896. Editor(s): Maia, Hernani L. S. ESCOM: Leiden, Neth.
CODEN: 63MBAO

DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 30 Oct 1996
AB Bacterial lipoproteins are synthesized as precursors with N-terminal signal sequences that are removed by enzymic cleavage during the multistep-processing of lipoproteins. The design and synthesis of synthetic substrates for measuring lipoprotein processing enzyme activity in an ELISA is reported. These substrates have the following features: (1) a biotinylated N-terminus to bind tightly on streptavidin-coated microtiter plates, (2) the consensus signal peptide sequence ILLAG, (3) Nε-2,4-dinitrophenyl-L-lysine for recognition by anti-Dnp antibodies in the ELISA, and (4) PEG or Ser-(Lys)4 to mediate water solubility Trypsin activity could be detected using one of the synthetic peptide substrates. This approach could provide a highly sensitive and exptl. simple method for the detection of enzymic activity.
CC 7-3 (Enzymes)
IT 182956-94-1P 182956-95-2P 182956-96-3P
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(as peptide substrate; combination of biotin, consensus signal peptide sequence, lipoamino acid, and antigenic Dnp-group in synthetic substrate for lipoprotein-processing proteinases)
IT 182956-96-3P
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(as peptide substrate; combination of biotin, consensus signal peptide sequence, lipoamino acid, and antigenic Dnp-group in synthetic substrate for lipoprotein-processing proteinases)
RN 182956-96-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, monoester with N-[6-[[6-[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]amino]-1-oxohexyl]amino]-1-oxohexyl]-β-alanyl-β-alanyl-L-isoleucyl-L-leucyl-L-leucyl-L-alanylglycyl-S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-L-cysteinyl-L-seryl-L-seryl-L-asparaginyl-N-[6-[[6-[[1-carboxy-5-[(2,4-dinitrophenyl)amino]pentyl]amino]-6-oxohexyl]amino]-6-oxohexyl]-L-alaninamide (9CI) (CA INDEX NAME)

PAGE 1-A



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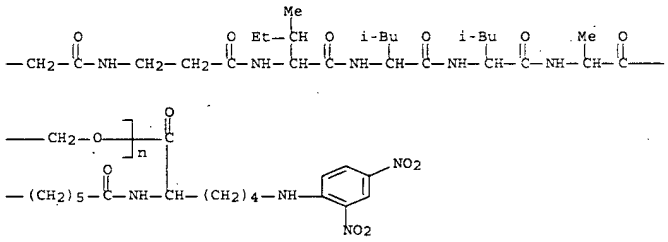

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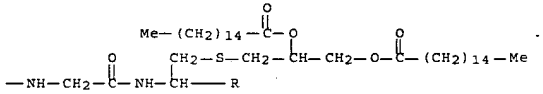


L12 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:438749 CAPLUS Full-text
DOCUMENT NUMBER: 125:112255
TITLE: Comparison of adjuvant formulations for cytotoxic T cell induction using synthetic peptides
AUTHOR(S): Hioe, Catarina E.; Qiu, Howard; Chend, Pei-De; Bian, Zuning; Li, Ming-Lie; Li, Joseph; Singh, Manmohan; Kuebler, Peter; McGee, Paul; et al.
CORPORATE SOURCE: Department Pathology, New York University, New York, NY, 10010, USA
SOURCE: Vaccine (1996), 14(5), 412-418
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Jul 1996
AB We have investigated the capacity of synthetic peptides delivered in different adjuvant formulations to induce cytotoxic T lymphocyte (CTL) responses to a class I H-2Kd-restricted Plasmodium berghei circumsporozoite epitope, CS 252-260. Using three immunogen formulations: soybean emulsion; Montanide ISA720; and lipopeptide (P3-CS), we first evaluated the effects of immunization routes on CTL induction. No CTL response was induced in mice immunized s.c. or i.p. with CS peptide formulated in soybean emulsion. In contrast, immunization with lipopeptide P3-CS either s.c. or i.p. effectively primed for CTL.

Interestingly, CS peptide emulsified in Montanide ISA720 induced a CTL response only when delivered s.c. and not i.p., indicating the critical influence of immunization routes on CTL induction. We then compared the effectiveness of eight adjuvant formulations to induce CTL response following a single s.c. immunization. Notably, lipopeptide P3-CS and CS peptide admixed with P3 or POE lipid mols. stimulated a vigorous CTL response. However, only mice immunized with P3-CS and CS peptide admixed with P3 mol. generated long-lived CTL which persisted in vivo for 5 mo. Thus, based on a simultaneous comparison of the different adjuvant formulations, we demonstrated that the conjugated and unconjugated P3 lipopeptides were the most effective immunogens for eliciting primary and memory CTL in mice.

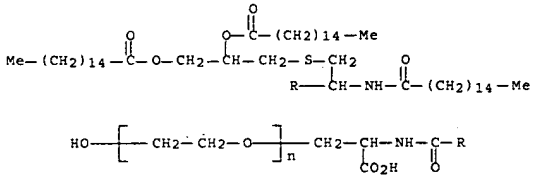
CC 15-2 (Immunochemistry)

IT 132957-09-6 160903-17-3, Montanide isa 720 178951-63-8 179091-76-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(comparison of adjuvant formulations for cytotoxic T cell induction using Plasmodium berghei circumsporozoite peptide)

IT 179091-76-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(comparison of adjuvant formulations for cytotoxic T cell induction using Plasmodium berghei circumsporozoite peptide)

RN 179091-76-0 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[2-[[3-[[2,3-bis[(1-oxohexadecyl)oxy]propyl]thio]-1-oxo-2-[(1-oxohexadecyl)amino]propyl]amino]-2-carboxyethyl]-ω-hydroxy-, [2R-[1(S*),2S*,2R*]]- (9CI) (CA INDEX NAME)



L12 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:546835 CAPLUS Full-text
DOCUMENT NUMBER: 122:291543
TITLE: Preparation of lipopeptides useful as drugs, in preparation of antibodies and vaccines, and in affinity chromatography.
INVENTOR(S): Rapp, Wolfgang; Jung, Guenther; Wiesmueller, Karl Heinz
PATENT ASSIGNEE(S): Rapp Polymere G.m.b.H., Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

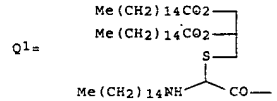
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4329309	A1	19950309	DE 1993-4329309	19930831
WO 9506484	A1	19950309	WO 1994-EP2838	19940826

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: DE 1993-4329309 A 19930831

ED Entered STN: 13 May 1995

GI



AB X(CH2CH2O)n-1CH2CH2YZp [X = OR1, SR1, NR1R2, +NR1R2R3, CO2R4, RX1; R = polymer matrix; X1 = divalent linker group; R1-R4 = H, PhCH2, alkyl; n = 5-500; Y = m-valent group; m ≥2; p = m-1; when p = 1, Z = adjuvant, peptide-adjuvant conjugate, or precursor thereof; the adjuvant portion cannot be larger than the peptide portion], having improved solubility properties, were prepared Thus, PAM3Cys-Leu-Leu-Gly-Ile-Leu-Glu-Ser-Arg-Gly- Lys-NH-POE-OMe (PAM3Cys = Q1; POE = polyoxyethylene) (solution phase preparation using FMOC-protected amino acids given) showed stimulation of T-helper cells in mice after foot pad immunization.

IC ICM C07K005-08
ICS C07K005-06; A61K038-06; C07K016-00; A61K039-395

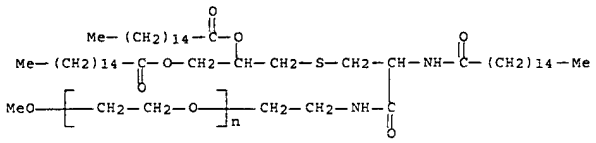
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 9, 15

IT 163006-58-4P 163006-59-5P 163006-60-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipopeptides useful as drugs, in preparation of antibodies and
vaccines, and in affinity chromatog.)

IT 163006-58-4P 163006-59-5P 163006-60-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipopeptides useful as drugs, in preparation of antibodies and
vaccines, and in affinity chromatog.)

RN 163006-58-4 CAPLUS

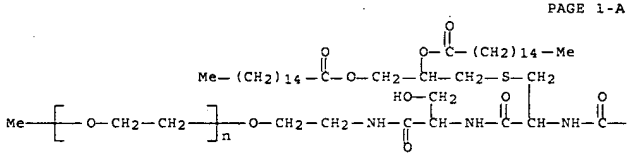
CN Poly(oxy-1,2-ethanediyl), α-[2-[[3-[[2,3-bis[(1-oxohexadecyl)oxy]propyl]thio]-1-oxo-2-[(1-oxohexadecyl)amino]propyl]amino]ethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



RN 163006-59-5 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, 2N-ether with S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-N-(1-oxohexadecyl)-L-cysteinyl-N-(2-hydroxyethyl)-L-serinamide (9CI) (CA INDEX NAME)

PAGE 1-A



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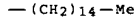
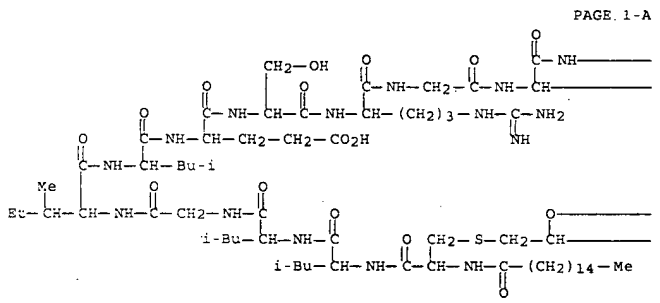


RN 163006-60-8 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy-, 11-ether with S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-N-(1-oxohexadecyl)-L-cysteinyl-L-leucyl-L-leucylglycyl-L-isoleucyl-L-leucyl-L-α-glutamyl-L-seryl-L-arginylglycyl-N-(2-hydroxyethyl)-L-lysinamide (9CI) (CA INDEX NAME)

PAGE 1-A



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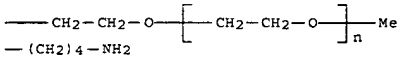
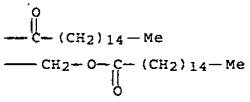




L12 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:595286 CAPLUS Full-text

DOCUMENT NUMBER: 121:195286

TITLE: Lipopeptide-polyoxyethylene conjugates as mitogens and adjuvants

AUTHOR(S): Kleine, Bernhard; Rapp, Wolfgang; Wiesmueller, Karl-Heinz; Edinger, Matthias; Beck, Werner; Metzger, Joerg; Ataulakhanov, Ravshan; Jung, Guenter; Bessler, Wolfgang G.

CORPORATE SOURCE: Inst. fur Immunbiologie, Univ. Freiburg, Freiburg/Br., Germany

SOURCE: Immunobiology (1994), 190(1-2), 53-66
CODEN: IMMND4; ISSN: 0171-2985

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 29 Oct 1994

AB Two lipopeptide analogs of the Escherichia coli lipoprotein rendered water-soluble by polyoxyethylene were tested for mitogenicity in vitro in murine and human B lymphocytes and for adjuvant activity in vivo in mice. These highly

amphiphilic lipopeptides retained the biol. activity other lipopeptides usually exerted which supports the hypothesis of specific interactions of lipopeptides with membranes of reactive cells. The activation of human B lymphocytes by these lipopeptides was much less pronounced compared to that of murine cells. However, given in combination with anti-CD40 antibodies plus interleukin-4, human B lymphocytes could synergistically be stimulated to proliferate. As an adjuvant, the polyoxyethylene-linked lipopeptides were almost as potent as Freund's adjuvants and other basic lipopeptides. Being water-soluble, these novel analogs are easy to apply and they are suitable for field studies as adjuvants when sonication can not usually be provided.

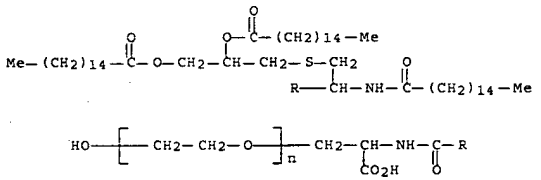
CC 1-7 (Pharmacology)
Section cross-reference(s): 15

IT 158010-70-9, 158010-71-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mitogenicity and adjuvant activity of)

IT 158010-70-9, 158010-71-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mitogenicity and adjuvant activity of)

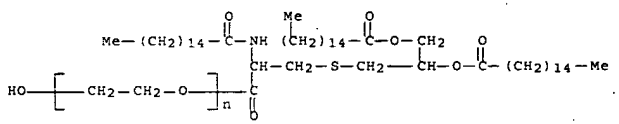
RN 158010-70-9 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[2-[[3-[[2,3-bis[(1-oxohexadecyl)oxy]propyl]thio]-1-oxo-2-[(1-oxohexadecyl)amino]propyl]amino]-2-carboxyethyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



RN 158010-71-0 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[3-[[2,3-bis[(1-oxohexadecyl)oxy]propyl]thio]-1-oxo-2-[(1-oxohexadecyl)amino]propyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



THE ESTIMATED COST FOR THIS REQUEST IS 72.91 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L25 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:947332 CAPLUS Full-text
DOCUMENT NUMBER: 147:275160
TITLE: The bacterial second messenger cdiGMP exhibits promising activity as a mucosal adjuvant
AUTHOR(S): Ebensen, Thomas; Schulze, Kai; Riese, Peggy; Morr, Michael; Guzman, Carlos A.
CORPORATE SOURCE: Department of Vaccinology, Helmholtz Centre for Infection Research, Braunschweig, D-38124, Germany
SOURCE: Clinical and Vaccine Immunology (2007), 14(8), 952-958
CODEN: CVILA6; ISSN: 1556-6811
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 27 Aug 2007

AB The development of mucosal adjuvants is still a critical need in vaccinol. In the present work, the authors show that bis(3',5')-cyclic dimeric GMP (cdiGMP), a second messenger that modulates cell surface properties of several microorganisms, exerts potent activity as a mucosal adjuvant. BALB/c mice were immunized intranasally with the model antigen β-galactosidase (β-Gal) coadministered with cdiGMP. Animals receiving cdiGMP as an adjuvant showed significantly higher anti-β-Gal IgG titers in sera than controls (i.e., 512-fold []). Coadministration of cdiGMP also stimulated efficient β-Gal-specific secretory IgA production in the lung and vagina. Cellular immune responses were observed in response to both the β-Gal protein and a peptide encompassing its major histocompatibility complex class I-restricted epitope. The IgG1-to-IgG2a ratio of anti-β-Gal anti-bodies and the observed profiles of secreted cytokines suggest that a dominant Th1 response pattern is promoted by mucosal coadministration of cdiGMP. Finally, the use of cdiGMP as a mucosal adjuvant also led to the stimulation of in vivo cytotoxic T-lymphocyte responses in C57BL/6 mice intranasally immunized with ovalbumin and cdiGMP (up to 30% of specific lysis). The results obtained indicate that cdiGMP is a promising tool for the development of mucosal vaccines.

CC 15-2 (Immunochemistry)

IT Immunostimulants
(adjuvants, mucosal; bacterial second messenger cdiGMP exhibits promising activity as a mucosal adjuvant)

IT Drug delivery systems
(nasal; bacterial second messenger cdiGMP exhibits promising activity as a mucosal adjuvant)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:558049 CAPLUS Full-text
DOCUMENT NUMBER: 146:528306
TITLE: New adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compositions
INVENTOR(S): Ebensen, Thomas; Guzman, Carlos, A.; Morr, Michael
PATENT ASSIGNEE(S): GBF Gesellschaft fuer Biotechnologische Forschung m.b.H., Germany
SOURCE: Eur. Pat. Appl., 33pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1787660	A1	20070523	EP 2005-25431	20051122
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
WO 2007059931	A1	20070531	WO 2006-EP11182	20061122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: EP 2005-25431 A 20051122
OTHER SOURCE(S): MARPAT 146:528306
ED Entered STN: 24 May 2007
AB The present invention relates to new adjuvants and the uses in pharmaceutical compns., like in vaccines. In particular, the present invention provides new conjugates of the bisacyloxycysteine type useful as adjuvants and/or immunomodulators for prophylactic and/or therapeutic vaccination in the treatment of infectious diseases, inflammatory diseases, autoimmune diseases, tumors, allergies as well as for the control of fertility in human or animal populations. The compds. are particularly useful not only as systemic, but preferably as mucosal adjuvants. In addition, the invention relates to its uses as active ingredients in pharmaceutical compns. The administration of BPPcysGlyc4armP EG triggered the induction of an efficient proliferative response at systemic (spleen cells) levels with high stimulation index.
CC 63-6 (Pharmaceuticals)
IT Allergy
Animal virus
Animalia
Animals
Autoimmune disease
Drug delivery systems
Human
Immunostimulants
Infection
Inflammation
Macrophage
Neoplasm
Preservatives
Spleen
Vaccines
(adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Immunostimulants
(adjuvants; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(injections, i.m.; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems

(injections, i.v.; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(liposomes; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(microparticles; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(mucosal; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(nanoparticles; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(nasal; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(oral; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(rectal; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(topical; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(vaginal; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
IT Drug delivery systems
(virosomes; adjuvants based on bisacyloxypropylcysteine conjugates and their uses in pharmaceutical compns.)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:502112 CAPLUS Full-text
DOCUMENT NUMBER: 146:480526
TITLE: Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control
INVENTOR(S): Ebensen, Thomas; Morr, Michael; Guzman, Carlos A.
PATENT ASSIGNEE(S): GBF Gesellschaft fuer Biotechnologische Forschung mbH, Germany
SOURCE: Eur. Pat. Appl., 43pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1782826	A1	20070509	EP 2005-24266	20051108
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
WO 2007054279	A2	20070518	WO 2006-EP10693	20061108

WO 2007054279 A3 20070830
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
WO 2007054283 A2 20070518 WO 2006-EP10699 20061108
WO 2007054283 A3 20070809
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRIORITY APPLN. INFO.: EP 2005-24266 A 20051108
OTHER SOURCE(S): MARPAT 146:480526
ED Entered STN: 09 May 2007
AB The present invention relates to new adjuvants and the uses in pharmaceutical compns., like in vaccines. In particular, the present invention provides new compds. useful as adjuvants and/or immunomodulators for prophylactic and/or therapeutic vaccination in the treatment of infectious diseases, inflammatory diseases, autoimmune diseases, tumors, allergies as well as for the control of fertility in human or animal populations. The compds. are particularly useful not only as systemic, but preferably as mucosal adjuvants. In addition, the invention relates to its uses as active ingredients in pharmaceutical compns.
CC 15-2 (Immunochemistry)
Section cross-reference(s): 63
IT Allergy
Allergy inhibitors
Angiogenesis inhibitors
Animalia
Animals
Anti-infective agents
Anti-inflammatory agents
Antitumor agents
Autoimmune disease
Contraceptives
Cytotoxic agents
Dendritic cell
Human
Immunomodulators
Immunostimulants
Infection
Inflammation
Macrophage
Neoplasm
Preservatives

Prophylaxis
Virus-like particle
(Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Immunostimulants
(adjuvants, ISCOMs; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Immunostimulants
(adjuvants; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(carriers; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(conjunctival; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(inhalants; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(injections, i.m.; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(injections, i.v.; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(injections, s.c.; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(intra NALT; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(intra-urethral; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(intrabronchial; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(intradermal; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(intrapulmonary; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune

disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(intrathecal; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(liposomes; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(microparticles; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(mucosal; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(nanoparticles; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(nasal, intra-; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(oral; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(parenterals; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(particles; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(polymer-bound; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(rectal, intra-; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Antitumor agents
(vaccines; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(vaginal, intra-; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
IT Drug delivery systems
(virosomes; Psudomonas quinolone signal and c-diGMP and conjugate as mucosal adjuvant for vaccine preparation against infection, autoimmune disease, inflammation, allergy, cancer and for fertility control)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:463101 CAPLUS Full-text
DOCUMENT NUMBER: 146:440188
TITLE: Hexosylceramides as adjuvants and their uses in pharmaceutical compositions
INVENTOR(S): Ebensen, Thomas; Morr, Michael; Guzman, Carlos A.
PATENT ASSIGNEE(S): GBF Gesellschaft fuer Biotechnologische Forschung Mbh, Germany
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007045469	A1	20070426	WO 2006-EP10086	20061019
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1776963	A1	20070425	EP 2005-22771	20051019
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: EP 2005-22771 A 20051019
OTHER SOURCE(S): MARPAT 146:440188
ED Entered STN: 27 Apr 2007
AB The present invention relates to new adjuvants and the uses in pharmaceutical compns., like in vaccines. In particular, the present invention provides new compds. useful as adjuvants for prophylactic and/or therapeutic vaccination in the treatment of infectious diseases, inflammatory diseases, autoimmune diseases, tumors, allergies as well as for the control of fertility in human or animal populations. The compds. are particularly useful not only as systemic, but preferably as mucosal adjuvants. In addition, the invention relates to its uses as active ingredients in pharmaceutical compns.
CC 15-2 (Immunochemistry)
Section cross-reference(s): 63
IT Immunostimulants
(adjuvants, ISCOMs; hexosylceramides as adjuvants and their use in vaccines)
IT Immunostimulants
(adjuvants; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(conjunctival; hexosylceramides as adjuvants and their use in vaccines)
IT Allergy
Angiogenesis inhibitors
Anti-inflammatory agents
Antigen presentation
Antigen-presenting cell

Autoimmune disease
Cytotoxic agents
Dendritic cell
Fertility
Human
Immunostimulants
Infection
Inflammation
Macrophage
Neoplasm
Vaccines
Virus-like particle
(hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(inhalants; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(injections, i.m.; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(injections, i.v.; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(injections, s.c.; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(intra-NALT; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(intra-urethral; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(intrabronchial; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(intradermal; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(intrapulmonary; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(intrathecal; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(liposomes; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(microparticles; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(mucosal; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(nanoparticles; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(nasal; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(oral; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(parenterals; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(rectal; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems
(vaginal; hexosylceramides as adjuvants and their use in vaccines)
IT Drug delivery systems

(virosomes; hexosylceramides as adjuvants and their use in vaccines)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:56703 CAPLUS Full-text
DOCUMENT NUMBER: 146:439918
TITLE: The bacterial second messenger cyclic diGMP exhibits potent adjuvant properties
AUTHOR(S): Ebensen, Thomas; Schulze, Kai; Riese, Peggy; Link, Claudia; Morr, Michael; Guzman, Carlos A.
CORPORATE SOURCE: Department of Vaccinology, Helmholtz Centre for Infection Research, Braunschweig, 38124, Germany
SOURCE: Vaccine (2007), 25(8), 1464-1469
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 18 Jan 2007
AB The identification of new adjuvants is a critical need in vaccinol. In this work, it is demonstrated that bis-(3',5')-cyclic dimeric guanosine monophosphate (cdiGMP) exhibits potent adjuvant properties. S.c. co-administration of cdiGMP with β-galactosidase (β-Gal) to mice resulted in the elicitation of significantly higher antigen-specific serum IgG titers than in animals receiving β-Gal alone. Strong cellular immune responses, which were characterized by a balanced Th1/Th2 pattern, were also observed in response to the β-Gal protein and a peptide encompassing its MHC class I-restricted epitope in immunized animals. These results suggest that cdiGMP represents a promising adjuvant for vaccine development.
CC 15-2 (Immunochemistry)
IT Immunostimulants
(adjuvants; co-administration of β-galactosidase with bacterial cdi-GMP elicit humoral and cellular response in mice)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:533958 CAPLUS Full-text
DOCUMENT NUMBER: 141:82330
TITLE: Methods using a lipopeptide or lipoprotein for treating lung infections and lung tumors and for treating and preventing lung metastases
INVENTOR(S): Muhlradt, Peter; Luhrmann, Anke; Tschernig, Thomas; Pabst, Reinhard
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 11 pp., Cont.-in-part of U.S. Ser. No. 398,094.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004127405	A1	20040701	US 2003-412547	20030411
DE 10048840	A1	20020411	DE 2000-10048840	20001002
WO 2002028887	A2	20020411	WO 2001-EP11414	20011002
WO 2002028887	A3	20021219		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2423897	A1	20041011	CA 2003-2423897		20030411
US 2004249133	A1	20041209	US 2003-398094		20030908
PRIORITY APPLN. INFO.:			DE 2000-10048840	A	20001002
			WO 2001-EP11414	W	20011002
			US 2003-398094	A	20030908
			US 2003-412547	A	20030411

OTHER SOURCE(S): MARPAT 141:82330
ED Entered STN: 02 Jul 2004
AB The invention discloses methods for treating lung infections and lung tumors and treating and preventing metastases of extrapulmonary tumors by administering lipopeptides or lipoproteins having the formula H2NCH[CH2XCH2CH*(OC(O)R2)CH2OC(O)R1]WYCOOH [R1, R2 = C 7-25 alkyl, C 7-25 alkenyl, C 7-25 alkynyl; X = S, O, CH2; W = CO, S(O)n; n = 1, 2; Y = physiol. acceptable amino acid sequence; * denotes asym. carbon atom].
IC ICM A61K038-17
ICS A61K038-10; C07K014-775
INCL 514012000; 514014000; 530359000
CC 1-9 (Pharmacology)
IT Drug delivery systems
(emulsions; lipopeptide or lipoprotein for treating lung infections and lung tumors and for treating and preventing lung metastases)
IT Drug delivery systems
(inhalants; lipopeptide or lipoprotein for treating lung infections and lung tumors and for treating and preventing lung metastases)
IT Antitumor agents
B cell (lymphocyte)
CD4-positive T cell
CD8-positive T cell
Dendritic cell
Lung, neoplasm
Lymphocyte
Macrophage
Monocyte
Neutrophil
T cell (lymphocyte)
(lipopeptide or lipoprotein for treating lung infections and lung tumors and for treating and preventing lung metastases)
IT Drug delivery systems
(solns.; lipopeptide or lipoprotein for treating lung infections and lung tumors and for treating and preventing lung metastases)
IT Drug delivery systems
(suspensions; lipopeptide or lipoprotein for treating lung infections and lung tumors and for treating and preventing lung metastases)

L25 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:367077 CAPLUS Full-text
DOCUMENT NUMBER: 141:5714
TITLE: The Toll-Like Receptor-2/6 Agonist Macrophage -Activating Lipopeptide-2 Cooperates with IFN-γ to Reverse the Th2 Skew in an In Vitro Allergy Model
AUTHOR(S): Weigt, Henning; Waldradt, Peter F.; Larbig,

Michael; Krug, Norbert; Braun, Armin
CORPORATE SOURCE: Department of Immunology, Allergology, and Clinical Inhalation, Fraunhofer Institute of Toxicology and Experimental Medicine, Hannover, Germany
SOURCE: Journal of Immunology (2004), 172(10), 6080-6086
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 May 2004
AB Dendritic cells (DC) are the most potent APCs with the capacity to induce, modulate, or shut down immune function. These features make them potentially useful for treating diseases associated with misled immunol. responses. Therefore, it was the aim of this study to reverse the allergen-dependent Th2 reaction responsible for allergic symptoms by modulating DC function. This issue was addressed in an in vitro test system consisting of human monocyte-derived allergen-pulsed DC from allergics cocultured with autologous lymphocytes. A Th2 reaction judged by the amplification of IL-4 and the down-regulation of IFN-γ was induced by pulsing DC with the relevant allergen. To modulate this reaction, the Toll-like receptor 2/6 engaging mycoplasmal lipopetide macrophage-activating lipopeptide 2 kDa was combined with IFN-γ to stimulate allergen-pulsed DC. Such treatment resulted in a 500-fold increase in IFN-γ production in the supernatant of cocultured autologous lymphocytes, while the Th2 marker IL-4 was not affected. This phenomenon was associated with an increase in proliferation and the number of IFN-γ-producing lymphocytes. Phenotype and function of thus treated DC remained stable. These data indicate that a former allergen-dependent Th2 reaction can be reversed toward a Th1-type response by an appropriate treatment of DC.
CC 15-9 (Immunochemistry)
IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD83; Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT Allergens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Der p 1 (Dermatophagoides pteronyssinus, 1); Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA-DR; Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT Cell proliferation
(T cell; Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TLR-2 (Toll-like receptor-2); Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 allergy model)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TLR-6 (Toll-like receptor-6); Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)

IT Allergy
Dendritic cell
Human
Monocyte
(Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT CD40 (antigen)
CD80 (antigen)
CD86 (antigen)
Interleukin 10
Interleukin 12
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT T cell (lymphocyte)
(helper cell/inducer, TH1; Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT T cell (lymphocyte)
(helper cell/inducer, TH2; Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT T cell (lymphocyte)
(proliferation; Toll-like receptor-2/6 agonist macrophage -activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ; Toll-like receptor-2/6 agonist macrophage -activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
IT 250718-44-6, MALP-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Toll-like receptor-2/6 agonist macrophage-activating lipopeptide-2 cooperates with IFN-γ to reverse the Th2 skew in an In vitro allergy model)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:499863 CAPLUS Full-text
DOCUMENT NUMBER: 139:83839
TITLE: Efficient mucosal delivery of the HIV-1 Tat protein using the synthetic lipopeptide MALP-2 as adjuvant
AUTHOR(S): Borsutzky, Stefan; Fiorelli, Valeria; Ebensen, Thomas; Tripiciano, Antonella; Rharbaoui, Faiza; Scoglio, Arianna; Link, Claudia; Nappi, Filomena; Morr, Michael; Butto, Stefano; Cafaro, Aurelio; Muehlradt, Peter F.; Ensoli, Barbara; Guzman, Carlos A.
CORPORATE SOURCE: Vaccine Research Group, Division of Microbiology, GBF-German Research Center for Biotechnology, Braunschweig, Germany
SOURCE: European Journal of Immunology (2003), 33(6), 1548-1556
CODEN: EJIMAF; ISSN: 0014-2980

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 01 Jul 2003
AB A major requirement for HIV/AIDS research is the development of a mucosal vaccine that stimulates humoral and cell-mediated immune responses at systemic and mucosal levels, thereby blocking virus replication at the entry port. Thus, a vaccine prototype based on biol. active HIV-1 Tat protein as antigen and the synthetic lipopeptide, macrophage-activating lipopeptide-2 (MALP-2), as a mucosal adjuvant was developed. Intranasal administration to mice stimulated systemic and mucosal anti-Tat antibody responses, and Tat-specific T cell responses, that were more efficient than those observed after i.p. immunization with Tat plus incomplete Freund's adjuvant. Major linear B cell epitopes mapped within aa 1-20 and 46-60, whereas T cell epitopes were identified within aa 36-50 and 56-70. These epitopes have also been described in vaccinated primates and in HIV-1-infected individuals with better prognosis. Anal. of the anti-Tat IgG isotypes in serum, and the cytokine profile of spleen cells indicated that a dominant Th1 helper response was stimulated by Tat plus MALP-2, as opposed to the Th2 response observed with Tat plus incomplete Freund's adjuvant. Tat-specific IFN-γ-producing cells were significantly increased only in response to Tat plus MALP-2. These data suggest that Malp-2 may represent an optimal mucosal adjuvant for candidate HIV vaccines based on Tat alone or in combination with other HIV antigens.
CC 15-8 (Immunochemistry)
Section cross-reference(s): 61
IT Lipopeptides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MALP-2 (macrophage-activating lipopeptide-2); efficient mucosal delivery of HIV-1 Tat protein using the synthetic lipopeptide MALP-2 as adjuvant)
IT Immunostimulants
(adjuvants; efficient mucosal delivery of HIV-1 Tat protein using the synthetic lipopeptide MALP-2 as adjuvant)
IT Drug delivery systems
(intranasal; efficient mucosal delivery of HIV-1 Tat protein using the synthetic lipopeptide MALP-2 as adjuvant)
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:3257 CAPLUS Full-text
DOCUMENT NUMBER: 138:88605
TITLE: Differential recognition of structural details of bacterial lipopeptides by toll-like receptors
AUTHOR(S): Morr, Michael; Takeuchi, Osamu; Akira, Shizuo; Simon, Markus M.; Muhlradt, Peter F.
CORPORATE SOURCE: Research Group Molecular Recognition of the Gesellschaft fur Biotechnologische Forschung, Braunschweig, Germany
SOURCE: European Journal of Immunology (2002), 32(12), 3337-3347
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 03 Jan 2003
AB The question which detailed structures of bacterial modulins determine their relative biol. activity and resp. host cell receptors was examined with synthetic variants of mycoplasmal lipopeptides as model compds., as well as

recombinant outer surface protein A (OspA) of Borrelia burgdorferi and lipoteichoic acid. Mouse fibroblasts bearing genetic deletions of various toll-like receptors (TLR) were the indicator cells to study receptor requirements, primary macrophages served to measure dose response. The following results were obtained: (i) the TLR system discriminates between modulins with three and those with two long-chain fatty acids in their lipid moiety, in that lipopeptides with three fatty acids were recognized by TLR2, whereas those with two long-chain fatty acids and lipoteichoic acid required the addnl. cooperation with TLR6; (ii) substitution of the free N terminus of mycoplasmal lipopeptides with an acetyl or palmitoyl group decreased the specific activity; (iii) removal of one or both ester-bound fatty acids lowered the specific activity by five orders of magnitude or deleted biol. activity; (iv) oxidation of the thioether group lowered the specific activity by at least four orders of magnitude. The implications of these findings for physiol. inactivation of lipopeptides and host-bacteria interactions in general are discussed.

CC 15-10 (Immunochemistry)

IT Borrelia burgdorferi
Macrophage
Structure-activity relationship
(recognition of bacterial lipopeptides by toll-like receptors)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:829325 CAPLUS Full-text
DOCUMENT NUMBER: 139:5262
TITLE: The Mycoplasma-derived lipopeptide MALP-2 is a potent mucosal adjuvant
AUTHOR(S): Rharbaoui, Faiza; Drabner, Birgit; Borsutzky, Stefan; Winckler, Urte; Morr, Michael; Ensoli, Barbara; Muhlradt, Peter F.; Guzman, Carlos A.
CORPORATE SOURCE: Vaccine Research Group, Division of Microbiology, GBF-German Research Center for Biotechnology, Braunschweig, D-38124, Germany
SOURCE: European Journal of Immunology (2002), 32(10), 2857-2865
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 31 Oct 2002

AB The adjuvanticity of MALP-2, a 2-kDa synthetic lipopeptide with macrophage-stimulatory activity, was evaluated in BALB/c mice using β-galactosidase (β-gal) as model antigen. When co-administered with β-gal by either the intranasal (i.n.) or i.p. route, MALP-2 (0.5 μg) was capable of increasing β-gal-specific serum IgG titers by 675-3560-fold (i.n.) and 64-128-fold (i.p.), resp., as compared to immunization with β-gal alone. Using MALP-2, almost maximal IgG responses were already stimulated following the first immunization, and the IgG titers were similar to those observed using 10 μg of cholera toxin B subunit (CTB) as adjuvant. The mucosal immune system was also effectively stimulated when MALP-2 was administered by the i.n. route (36% and 23% of β-gal-specific IgA in lung and vaginal lavages, resp.). The i.n. co-administration of MALP-2 stimulated a stronger cellular immune response than CTB, both in submandibular lymph nodes and spleen. The anal. of β-gal-specific IgG isotypes and the profiles of cytokines secreted by in vitro re-stimulated cells showed that co-administration of MALP-2 triggered a dominant Th2-response pattern. A recruitment of B220+ and MAC-1+ cells with an up-

regulated expression of MHC class I, CD80 (B7.1) and CD54 (ICAM-1) was observed in nasal associated lymphoid tissues from MALP-2 treated mice. Taken together, the results demonstrated that the synthetic lipopeptide MALP-2 represents a very promising adjuvant for the mucosal delivery of vaccine antigens.

CC 15-2 (Immunochemistry)

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD54; up-regulation on monocytes/macrophages by synthetic Mycoplasma-derived lipopeptide MALP-2)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H-2, class I; up-regulation on monocytes/macrophages by synthetic Mycoplasma-derived lipopeptide MALP-2)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICAM-1 (intercellular adhesion mol. 1); up-regulation on monocytes/macrophages by synthetic Mycoplasma-derived lipopeptide MALP-2)

IT Macrophage
Monocyte
(stimulation in mucosal lymphoid tissue by synthetic Mycoplasma-derived lipopeptide MALP-2)

IT CD80 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(up-regulation on monocytes/macrophages by synthetic Mycoplasma-derived lipopeptide MALP-2)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:489723 CAPLUS Full-text
DOCUMENT NUMBER: 137:91745
TITLE: In vivo effects of a synthetic 2-kilodalton macrophage-activating lipopeptide of Mycoplasma fermentans after pulmonary application
AUTHOR(S): Luhrmann, Anke; Deiters, Ursula; Skokowa, Julia; Hanke, Michaela; Gessner, Johannes E.; Muhlradt, Peter F.; Pabst, Reinhard; Tschernig, Thomas
CORPORATE SOURCE: Departments of Functional and Applied Anatomy, Medical School of Hannover, Hannover, 30623, Germany
SOURCE: Infection and Immunity (2002), 70(7), 3785-3792
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Jun 2002

AB Mycoplasmas can cause interstitial pneumonias inducing critical illness in humans and animals. Mycoplasma infections are characterized by an influx of neutrophils, followed by an accumulation of macrophages and lymphocytes. The present study deals with the question of which mycoplasmal components cause this host reaction. The mycoplasma-derived, macrophage-activating lipopeptide 2S-MALP-2 was used to mimic the sequelae of a mycoplasma infection. To this end, 2S-MALP-2 was intratracheally instilled into the lungs of Lewis rats, and the bronchoalveolar lavage cells were examined at different times after different doses of 2S-MALP-2. Application of 2.5 μg induced a pronounced leukocyte accumulation in the bronchoalveolar space. At 24 h after 2S-MALP-2 administration, the majority of leukocytes consisted of neutrophils, followed by macrophages, peaking on days 2 and 3. Lymphocyte nos., although amounting to only a few percent of the total bronchoalveolar lavage cells, also increased significantly, with maximal lymphocyte accumulation occurring by 72

h after instillation. The leukocyte count of the lung interstitium was increased on day 3 after treatment. After 10 days all investigated cell populations returned to control levels. Transient chemotactic activity for neutrophils was detected in the bronchoalveolar lavage fluid early after 2S-MALP-2 application, followed by monocyte chemoattractant protein-1 activity (MCP-1) in lung homogenates. MCP-1 was produced by bronchoalveolar lavage cells upon stimulation with 2S-MALP-2. Our data indicate that mycoplasmal lipoproteins and lipopeptides are probably the most relevant mycoplasmal components for the early host reaction. The primary target cells are likely to be the alveolar macrophages liberating chemokines, which attract further leukocytes.

CC 14-3 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 10, 15

ST macrophage activating lipopeptide Mycoplasma lung leukocyte accumulation

IT Lipopeptides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MALP-2; leukocyte infiltration response to macrophage -activating lipopeptide of Mycoplasma fermentans)

IT Lymphocyte
Neutrophil
(accumulation in response to macrophage-activating lipopeptide of Mycoplasma fermentans)

IT Macrophage
(alveolar; accumulation in response to macrophage-activating lipopeptide of Mycoplasma fermentans)

IT Monocyte chemoattractant protein-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression in inflammatory response to macrophage-activating lipopeptide of Mycoplasma fermentans)

IT Leukocyte
(infiltration; in response to macrophage-activating lipopeptide of Mycoplasma fermentans)

IT Mycoplasma fermentans
(leukocyte infiltration response to macrophage-activating lipopeptide of)

IT Pneumonia
(leukocyte infiltration response to macrophage-activating lipopeptide of Mycoplasma fermentans)

IT Cell migration
(leukocyte infiltration; in response to macrophage-activating lipopeptide of Mycoplasma fermentans)

IT Lung
(macrophage; accumulation in response to macrophage -activating lipopeptide of Mycoplasma fermentans)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:832589 CAPLUS Full-text
DOCUMENT NUMBER: 136:117118
TITLE: Lipopolysaccharide stimulates the MyD88-independent pathway and results in activation of IFN-regulatory factor 3 and the expression of a subset of lipopolysaccharide-inducible genes
AUTHOR(S): Kawai, Taro; Takeuchi, Osamu; Fujita, Takashi; Inoue, Jun-Ichiro; Muhlradt, Peter F.; Sato, Shintaro; Hoshino, Katsuaki; Akira, Shizuo
CORPORATE SOURCE: Department of Host Defense, Research Institute for Microbial Diseases and Core Research for Evolutional

Science and Technology, Japan Science and Technology Corporation, Osaka University, Osaka, Japan
SOURCE: Journal of Immunology (2001), 167(10), 5887-5894
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 16 Nov 2001
AB Bacterial lipopolysaccharide (LPS) triggers innate immune responses through Toll-like receptor (TLR) 4, a member of the TLR family that participates in pathogen recognition. TLRs recruit a cytoplasmic protein, MyD88, upon pathogen recognition, mediating its function for immune responses. Two major pathways for LPS have been suggested in recent studies, which are referred to as MyD88-dependent and -independent pathways. We report in this study the characterization of the MyD88-independent pathway via TLR4. MyD88-deficient cells failed to produce inflammatory cytokines in response to LPS, whereas they responded to LPS by activating IFN-regulatory factor 3 as well as inducing the genes containing IFN-stimulated regulatory elements such as IP-10. In contrast, a lipopeptide that activates TLR2 had no ability to activate IFN-regulatory factor 3. The MyD88-independent pathway was also activated in cells lacking both MyD88 and TNFR-associated factor 6. Thus, TLR4 signaling is composed of at least two distinct pathways, a MyD88-dependent pathway that is critical to the induction of inflammatory cytokines and a MyD88/TNFR-associated factor 6-independent pathway that regulates induction of IP-10.
CC 15-5 (Immunochemistry)
IT Macrophage
Signal transduction, biological
(lipopolysaccharide stimulates MyD88/TRAF6-independent pathway and results in activation of IFN-regulatory factor 3 and expression of a subset of lipopolysaccharide-inducible genes)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:557379 CAPLUS Full-text
DOCUMENT NUMBER: 135:256104
TITLE: Discrimination of bacterial lipoproteins by Toll-like receptor 6
AUTHOR(S): Takeuchi, Osamu; Kawai, Taro; Muhlradt, Peter F.; Morr, Michael; Radolf, Justin D.; Zychlinsky, Arturo; Takeda, Kiyoshi; Akira, Shizuo
CORPORATE SOURCE: Department of Host Defense, Research Institute for Microbial Diseases, Osaka University, and Core Research for Evolutional Science and Technology (CREST) of Japan Science and Technology Corp., Suita, 565-0871, Japan
SOURCE: International Immunology (2001), 13(7), 933-940
CODEN: INIMEN; ISSN: 0953-8178
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 Aug 2001
AB Bacterial lipoproteins (BLP) trigger immune responses via Toll-like receptor 2 (TLR2) and their immunostimulatory properties are attributed to the presence of a lipoylated N-terminus. Most BLP are triacylated at the N-terminus cysteine residue, but mycoplasmal macrophage-activating lipopeptide-2 kDa (MALP-2) is only diacylated. Here the authors show that TLR6-deficient (TLR6-/-) cells are unresponsive to MALP-2 but retain their normal responses to lipopeptides of other bacterial origins. Reconstitution expts. in TLR2-/-TLR6-/- embryonic fibroblasts reveal that co-expression of TLR2 and TLR6 is

absolutely required for MALP-2 responsiveness. Taken together, these results show that TLR6 recognizes MALP-2 cooperatively with TLR2, and appears to discriminate between the N-terminal lipoylated structures of MALP-2 and lipopeptides derived from other bacteria.

CC 15-10 (Immunochemistry)

IT Lipopeptides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MALP-2 (macrophage-activating lipopeptide-2); Toll-like receptor-6 mediates recognition of)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:898315 CAPLUS Full-text
DOCUMENT NUMBER: 134:161769
TITLE: Synergy and cross-tolerance between toll-like receptor (TLR) 2- and TLR4-mediated signaling pathways
AUTHOR(S): Sato, Shintaro; Nomura, Fumiko; Kawai, Taro; Takeuchi, Osamu; Muhlradt, Peter F.; Takeda, Kiyoshi; Akira, Shizuo
CORPORATE SOURCE: Department of Host Defense, Research Institute for Microbial Diseases, Osaka University, Osaka, 565-0871, Japan
SOURCE: Journal of Immunology (2000), 165(12), 7096-7101
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Dec 2000

AB A family of Toll-like receptor (TLR) mediates the cellular response to bacterial cell wall components; murine TLR2 and TLR4 recognize mycoplasmal lipopeptides (macrophage-activating lipopeptides, 2 kDa (MALP-2)) and LPS, resp. Costimulation of mouse peritoneal macrophages with MALP-2 and LPS results in a marked increase in TNF-α production, showing the synergy between TLR2- and TLR4-mediated signaling pathways. Macrophages pretreated with LPS show hyporesponsiveness to the second LPS stimulation, termed LPS tolerance. The LPS tolerance has recently been shown to be primarily due to the down-regulation of surface expression of the TLR4-MD2 complex. When macrophages were treated with MALP-2, the cells showed hyperresponsiveness to the second MALP-2 stimulation, like LPS tolerance. Furthermore, macrophages pretreated with MALP-2 showed reduced production of TNF-α in response to LPS. LPS-induced activation of both NF-κB and c-Jun NH2-terminal kinase was severely impaired in MALP-2-pretreated cells. However, MALP-2-pretreated macrophages did not show any reduction in surface expression of the TLR4-MD2 complex. These findings indicate that LPS-induced LPS tolerance mainly occurs through the down-regulation of surface expression of the TLR4-MD2 complex; in contrast, MALP-2-induced LPS tolerance is due to modulation of the downstream cytoplasmic signaling pathways.

CC 15-8 (Immunochemistry)

IT Lipopeptides
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MALP-2 (macrophage-activating lipopeptide 2); synergy and cross-tolerance between toll-like receptor (TLR) 2- and TLR4-mediated signaling pathways and response to)

IT Macrophage
(synergy and cross-tolerance between toll-like receptor (TLR) 2- and TLR4-mediated signaling pathways effect on)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:52425 CAPLUS Full-text
DOCUMENT NUMBER: 132:206889
TITLE: Cutting edge: preferentially the R-stereoisomer of the mycoplasmal lipopeptide macrophage -activating lipopeptide-2 activates immune cells through a toll-like receptor 2- and MyD88-dependent signaling pathway
AUTHOR(S): Takeuchi, Osamu; Kaufmann, Andreas; Grote, Karsten; Kawai, Taro; Hoshino, Katsuaki; Morr, Michael ; Muhlradt, Peter F.; Akira, Shizuo
CORPORATE SOURCE: Department of Host Defense, Research Institute for Microbial Diseases, Osaka University, Osaka, 565-0871, Japan
SOURCE: Journal of Immunology (2000), 164(2), 554-557
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Jan 2000

AB Mycoplasmas and their membranes are potent activators of macrophages, the active principle being lipoproteins and lipopeptides. Two stereoisomers of the mycoplasmal lipopeptide macrophage-activating lipopeptide-2 (MALP-2) differing in the configuration of the lipid moiety were synthesized and compared in their macrophage-activating potential, the R-MALP being >100 times more active than the S-MALP in stimulating the release of cytokines, chemokines, and NO. To assess the role of the Toll-like receptor (TLR) family in mycoplasmal lipopeptide signaling, the MALP-2-mediated responses were analyzed using macrophages from wild-type, TLR2-, TLR4-, and MyD88-deficient mice. TLR2- and MyD88-deficient cells showed severely impaired cytokine productions in response to R- and S-MALP. The MALP-induced activation of intracellular signaling mols. was fully dependent on both TLR2 and MyD88. There was a strong preference for the R-MALP in the recognition by its functional receptor, TLR2.

CC 15-10 (Immunochemistry)

ST Mycoplasma MALP2 macrophage activation TLR2 MyD88 signaling

IT Lipopeptides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(MALP-2 (macrophage-activating lipopeptide-2); R- vs. S-stereoisomers of mycoplasmal lipopeptide MALP-2 and macrophage activation through a Toll-like receptor 2- and MyD88-dependent signaling pathway)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MyD88; R- vs. S-stereoisomers of mycoplasmal lipopeptide MALP-2 and macrophage activation through a Toll-like receptor 2- and MyD88-dependent signaling pathway)

IT Cell membrane
Mycoplasma
Signal transduction, biological
(R- vs. S-stereoisomers of mycoplasmal lipopeptide MALP-2 and macrophage activation through a Toll-like receptor 2- and MyD88-dependent signaling pathway)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(TLR-2 (Toll-like receptor-2); R- vs. S-stereoisomers of mycoplasmal lipopeptide MALP-2 and macrophage activation through a Toll-like receptor 2- and MyD88-dependent signaling pathway)

IT Macrophage
(activation; R- vs. S-stereoisomers of mycoplasmal lipopeptide MALP-2 and macrophage activation through a Toll-like receptor 2- and MyD88-dependent signaling pathway)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:768674 CAPLUS Full-text
DOCUMENT NUMBER: 132:62973
TITLE: Induction of cytokines and chemokines in human monocytes by Mycoplasma fermentans-derived lipoprotein MALP-2
AUTHOR(S): Kaufmann, A.; Muhlradt, P. F.; Gemsa, D.; Sprenger, H.
CORPORATE SOURCE: Institute of Immunology, Philipps University, Marburg, D-35037, Germany
SOURCE: Infection and Immunity (1999), 67(12), 6303-6308
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Dec 1999
AB Bacterial infections are characterized by strong inflammatory reactions. The responsible mediators are often bacterially derived cell wall mols., such as lipopolysaccharide or lipoteichoic acids, which typically stimulate monocytes and macrophages to release a wide variety of inflammatory cytokines and chemokines. Mycoplasmas, which lack a cell wall, may also stimulate monocytes very efficiently. This study was performed to identify mycoplasma-induced mediators. The authors investigated the induction of cytokines and chemokines in human monocytes exposed to the Mycoplasma fermentans-derived membrane component MALP-2 (macrophage-activating lipopeptide 2) by dose response and kinetic anal. The authors found a rapid and strong MALP-2-inducible chemokine and cytokine gene expression which was followed by the release of chemokines and cytokines with peak levels after 12 to 20 h. MALP-2 induced the neutrophil-attracting CXC chemokines interleukin-8 (IL-8) and GRO-α as well as the mononuclear leukocyte-attracting CC chemokines MCP-1, MIP-1α, and MIP-1β. Production of the proinflammatory cytokines tumor necrosis factor alpha and IL-6 started at the same time as chemokine release but required 10- to 100-fold-higher MALP-2 doses. The data show that the mycoplasma-derived lipopeptide MALP-2 represents a potent inducer of chemokines and cytokines which may, by the attraction and activation of neutrophils and mononuclear leukocytes, significantly contribute to the inflammatory response during mycoplasma infection.
CC 15-5 (Immunochemistry)
IT Lipoproteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MALP-2 (macrophage-activating lipopeptide 2); Mycoplasma fermentans MALP-2 lipoprotein induces proinflammatory cytokine and chemokine expression by human monocytes)
IT Interleukin 6
Interleukin 8
Macrophage inflammatory protein 1α
Macrophage inflammatory protein 1β

Melanoma growth-stimulating activity-α
Monocyte chemoattractant protein-1
Tumor necrosis factors
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(Mycoplasma fermentans MALP-2 lipoprotein induces proinflammatory cytokine and chemokine expression by human monocytes)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:768671 CAPLUS Full-text
DOCUMENT NUMBER: 132:76899
TITLE: Effect of MALP-2, a lipopeptide from Mycoplasma fermentans, on bone resorption in vitro
AUTHOR(S): Piec, Grazyna; Mirkovitch, Jelena; Palacio, Silvia; Muhlradt, Peter F.; Felix, Rolf
CORPORATE SOURCE: Department of Clinical Research, Bone Biology, University of Bern, Bern, CH-3010, Switz.
SOURCE: Infection and Immunity (1999), 67(12), 6281-6285
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Dec 1999
AB Mycoplasmas may be associated with rheumatoid arthritis in various animal hosts. In humans, mycoplasma arthritis has been recorded in association with hypogammaglobulinemia. Mycoplasma fermentans is one mycoplasma species considered to be involved in causing arthritis. To clarify which mycoplasmal compds. contribute to the inflammatory, bone-destructive processes in arthritis, we used a well-defined lipopeptide, 2-kDa macrophage-activating lipopeptide (MALP-2) from M. fermentans, as an example of a class of macrophage-activating compds. ubiquitous in mycoplasmas, to study its effects on bone resorption. MALP-2 stimulated osteoclast-mediated bone resorption in murine calvaria cultures, with a maximal effect at around 2 nM. Anti-inflammatory drugs inhibited MALP-2-mediated bone resorption by about 30%. This finding suggests that MALP-2 stimulates bone resorption partially by stimulating the formation of prostaglandins. Since interleukin-6 (IL-6) stimulates bone resorption, we investigated IL-6 production in cultured calvaria. MALP-2 stimulated the liberation of IL-6, while no tumor necrosis factor was detectable. Addnl., MALP-2 stimulated low levels of NO in calvaria cultures, an effect which was strongly increased in the presence of gamma interferon, causing an inhibition of bone resorption. MALP-2 stimulated the bone-resorbing activity of osteoclasts isolated from long bones of newborn rats and cultured on dentin slices without affecting their number In bone marrow cultures, MALP-2 inhibited the formation of osteoclasts. It appears that MALP-2 has two opposing effects: it increases the bone resorption in bone tissue by stimulation of mature osteoclasts but inhibits the formation of new ones.
CC 14-3 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 15
IT Lipoproteins
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MALP-2 (macrophage-activating lipopeptide 2); MALP-2, a lipopeptide from Mycoplasma fermentans, effect on bone resorption in vitro)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:412224 CAPLUS Full-text
DOCUMENT NUMBER: 131:198535
TITLE: Mycoplasmal lipopeptide MALP-2 induces the chemoattractant proteins macrophage inflammatory protein 1α (MIP-1α), monocyte chemoattractant protein 1, and MIP-2 and promotes leukocyte infiltration in mice
AUTHOR(S): Deiters, Ursula; Muhlradt, Peter F.
CORPORATE SOURCE: Immunobiology Research Group, Gesellschaft fur Biotechnologische Forschung mbH, Braunschweig, D-38124, Germany
SOURCE: Infection and Immunity (1999), 67(7), 3390-3398
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Jul 1999
AB Natural as well as exptl. infections with pathogenic mycoplasmas lead to cellular responses characterized by early polymorphonuclear leukocyte influx, which in turn is followed by infiltration of macrophages. Since some of the most potent leukocyte chemoattractants are macrophage products, the authors investigated whether the 2-kDa macrophage-activating lipopeptide (MALP-2) from Mycoplasma fermentans was capable of inducing chemoattractant chemokines and initiating an in vivo inflammatory effect. MALP-2 was a potent in vitro inducer of the chemokines macrophage inflammatory protein 1α (MIP-1α), monocyte chemoattractant protein 1 (MCP-1), and MIP-2, yielding a maximal response at 0.1 ng/mL (5+10-11 M). Leukocyte infiltration was determined after i.p. injection of MALP-2, liposome-encapsulated MALP-2, and heat-killed mycoplasmas. There was a steady increase in the number of peritoneal cells over 72 h in response to these agents. Polymorph counts were maximal by 24-48 h, decreasing thereafter. Monocytes/macrophages had increased after 3 days. MIP-1α, MCP-1, and MIP-2 levels in serum or peritoneal lavage fluid were determined MIP-1α and MCP-1 levels were elevated by 2-6 h after injection and were still above control values after 24 h. In contrast, MIP-2 levels reached their maximum at 2 h, dropping to control values after 24 h. Thus, macrophage-stimulating mycoplasmal lipoproteins, exemplified by MALP-2, play an important role in the late phase of phagocyte recruitment at sites of infection and this is affected by leukoattractive chemokines.
CC 15-8 (Immunochemistry)
Section cross-reference(s): 63
IT Lipopeptides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MALP-2 (macrophage-activating lipopeptide-2); mycoplasmal lipopeptide MALP-2 induces formation of chemoattractant proteins MIP-1α, monocyte chemoattractant protein 1, and MIP-2 and promotes leukocyte infiltration)
IT Macrophage
(infiltration; mycoplasmal lipopeptide MALP-2 induces formation of chemoattractant proteins MIP-1α, monocyte chemoattractant protein 1, and MIP-2 and promotes leukocyte infiltration)
IT Drug delivery systems
(liposomes; liposome-encapsulated mycoplasmal lipopeptide MALP-2 induces formation of chemoattractant proteins MIP-1α, monocyte chemoattractant protein 1, and MIP-2 and promotes leukocyte infiltration)
IT Macrophage inflammatory protein 1α

Monocyte chemoattractant protein-1
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(mycoplasmal lipopeptide MALP-2 induces formation of chemoattractant proteins MIP-1α, monocyte chemoattractant protein 1, and MIP-2 and promotes leukocyte infiltration)
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:83299 CAPLUS Full-text
DOCUMENT NUMBER: 130:293743
TITLE: Differential posttranslational processing confers intraspecies variation of a major surface lipoprotein and a macrophage-activating lipopeptide of Mycoplasma fermentans
AUTHOR(S): Calcutt, Michael J.; Kim, Mary F.; Karpas, Arthur B.; Muhlradt, Peter F.; Wise, Kim S.
CORPORATE SOURCE: Department of Molecular Microbiology and Immunology, School of Medicine, University of Missouri-Columbia, Columbia, MO, 65212, USA
SOURCE: Infection and Immunity (1999), 67(2), 760-771
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Feb 1999
AB The malp gene of Mycoplasma fermentans is shown to occur in single copy but to encode two discrete translated forms of lipid-modified surface protein that can be differentially expressed on isolates within this species: MALP-2, a 14-amino-acid (2-kDa) lipopeptide with potent macrophage-stimulatory activity (P. F. Muhlradt, M. Kiess, H. Meyer, R. Sussmuth, and G. Jung, J. Exp. Med. 185:1951-1958, 1997), and MALP-404, an abundant, full-length (404-amino-acid) surface lipoprotein of 41 kDa, previously designated P41 (K. S. Wise, M. F. Kim, P. M. Theiss, and S.-C. Lo, Infect. Immun. 61:3327-3333, 1993). The sequences, transcripts, and translation products of malp were compared between clonal isolates of strains PG18 (known to express P41) and II-29/1 (known to express high levels of MALP-2). Despite conserved malp DNA sequences containing full-length open reading frames and expression of full-length monocistronic transcripts in both isolates, Western blotting using a monoclonal antibody (MAb) to the N-terminal MALP-2 peptide revealed marked differences in the protein products expressed. Whereas PG18 expressed abundant MALP-404 with detectable MALP-2, II-29/1 revealed no MALP-404 even in samples containing a large comparative excess of MALP-2. Colony immunoblots with the MAb showed uniform surface expression of MALP-2 in II-29/1 populations. A second MAb to an epitope of MALP-404 outside the MALP-2 sequence predictably failed to stain II-29/1 colonies but uniformly stained PG18 populations. Collectively, these results provide evidence for novel post-transcriptional (probably posttranslational) processing pathways leading to differential intraspecies expression of a major lipoprotein, and a potent macrophage-activating lipopeptide, on the surface of M. fermentans. In the course of this study, a striking conserved motif (consensus, TD-G--DDKSFNQSAWE--), designated SLA, was identified in MALP-404; this motif is also distributed among selected lipoproteins and species from diverse bacterial genera, including Bacillus, Borrelia, Listeria, Mycoplasma, and Treponema. In addition, malp was shown to flank a chromosomal polymorphism. In eight isolates of M. fermentans examined, malp occurred upstream of an operon encoding the phase-variable P78 ABC transporter; but, in three of these isolates, a newly discovered insertion sequence, IS1630 (of the IS30 class), was located between these genes.

CC 10-2 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 3, 6, 15
IT Lipopeptides
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative)
(MALP-2; differential posttranslational processing of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
IT Lipoproteins
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative)
(MALP-404; differential posttranslational processing of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
IT DNA sequences
Protein sequences
(differential posttranslational processing confers intraspecies variation of a major surface lipoprotein and a macrophage -activating lipopeptide of Mycoplasma fermentans)
IT Mycoplasma fermentans
(differential posttranslational processing of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
IT Gene, microbial
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(malp; differential posttranslational processing of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
IT Post-translational processing
(of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
IT Enzymes, properties
RL: PRP (Properties)
(transposases; differential posttranslational processing of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
IT 192394-37-9 192394-38-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; differential posttranslational processing confers intraspecies variation of a major surface lipoprotein and a macrophage-activating lipopeptide of Mycoplasma fermentans)
IT 223118-39-6 223118-49-8 223118-50-1 223118-51-2 223118-57-8
223118-62-5
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(amino acid sequence; differential posttranslational processing of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
IT 192394-36-8 223118-46-5 223118-47-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; differential posttranslational processing of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
IT 192394-44-8 223118-36-3 223118-37-4 223118-38-5 223118-40-9
RL: PRP (Properties)
(amino acid sequence; differential posttranslational processing of major surface lipoprotein and macrophage-activating

lipopeptide of Mycoplasma fermentans)
IT 9000-83-3, ATPase 37217-33-7, DNA polymerase III
RL: PRP (Properties)
(differential posttranslational processing of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
IT 222389-95-9, GenBank AF099209 222389-96-0, GenBank AF099210
222389-97-1, GenBank AF099211 222389-98-2, GenBank AF099212
222389-99-3, GenBank AF099213 222390-00-3, GenBank AF099214
222390-06-9, GenBank AF100324
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; differential posttranslational processing of major surface lipoprotein and macrophage-activating lipopeptide of Mycoplasma fermentans)
REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:649612 CAPLUS Full-text
DOCUMENT NUMBER: 130:24072
TITLE: Structure and specific activity of macrophage -stimulating lipopeptides from Mycoplasma hyorhinis
AUTHOR(S): Muhlradt, Peter F.; Kiess, Michael; Meyer, Holger; Sussmuth, Roderich; Jung, Gunther
CORPORATE SOURCE: Immunobiology and Structure Research Groups, Gesellschaft fur Biotechnologische Forschung mbH, Braunschweig, D-38124, Germany
SOURCE: Infection and Immunity (1998), 66(10), 4804-4810
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 14 Oct 1998
AB Mycoplasmas are potent macrophage stimulators. We describe the isolation of macrophage-stimulatory lipopeptides S-[2,3-bisacyl(C16:0/C18:0)oxypropyl]cysteinyl-GQTDNNSSQSQQPGSGTTNT and S-[2,3-bisacyl (C16:0/C18:0)oxypropyl]cysteinyl-GQTN derived from the Mycoplasma hyorhinis variable lipoproteins VlpA and VlpC, resp. These lipopeptides were characterized by amino acid sequence and composition anal. and by mass spectrometry. The lipopeptides S-[2,3- bis(palmitoyloxy)propyl]cysteinyl-GQTNT and S-[2,3- bis(palmitoyloxy)propyl]cysteinyl-SKKKK and the N-palmitoylated derivative of the latter were synthesized, and their macrophage-stimulatory activities were compared in a nitric oxide release assay with peritoneal macrophages from C3H/HeJ mice. The lipopeptides with the free amino terminus showed half-maximal activity at 3 pM regardless of their amino acid sequence; i.e., they were as active as the previously isolated M. fermentans-derived lipopeptide MALP-2. The macrophage-stimulatory activity of the addnl. N-palmitoylated lipopeptide or of the murein lipoprotein from Escherichia coli, however, was lower by orders of magnitude. It is concluded that the lack of N-acyl groups in mycoplasmal lipoproteins explains their exceptionally high in vitro macrophage-stimulatory capacity. Certain features that lipopolysaccharide endotoxin and mycoplasmal lipopeptides have in common are discussed. Lipoproteins and lipopeptides are likely to be the main causative agents of inflammatory reactions to mycoplasmas. This may be relevant in the context of mycoplasmas as arthritogenic pathogens and their association with AIDS.
CC 15-10 (Immunochemistry)
ST Mycoplasma macrophage stimulating lipopeptide
IT Protein sequences

(amino acid sequences of macrophage-stimulating lipopeptides from Mycoplasma hyorhinis)

IT Lipopolysaccharides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bacterial; structure and specific activity of macrophage -stimulating lipopeptides from Mycoplasma hyorhinis in relation to lipopolysaccharides from gram-neg. bacteria)

IT Structure-activity relationship
(macrophage-stimulating; of macrophage-stimulating lipopeptides from Mycoplasma hyorhinis)

IT Peritoneum
(macrophage; structure and specific activity of macrophage-stimulating lipopeptides from Mycoplasma hyorhinis)

IT Macrophage
(peritoneal; structure and specific activity of macrophage -stimulating lipopeptides from Mycoplasma hyorhinis)

IT Mycoplasma hyorhinis
(structure and specific activity of macrophage-stimulating lipopeptides from Mycoplasma hyorhinis)

IT Lipopeptides
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(structure and specific activity of macrophage-stimulating lipopeptides from Mycoplasma hyorhinis)

IT Gram-negative bacteria
(structure and specific activity of macrophage-stimulating lipopeptides from Mycoplasma hyorhinis in relation to lipopolysaccharides from gram-neg. bacteria)

IT 216300-10-6DP, acyl derivs. 216300-11-7DP, acyl derivs.
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(structure and specific activity of macrophage-stimulating lipopeptides from Mycoplasma hyorhinis)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:560269 CAPLUS Full-text
DOCUMENT NUMBER: 127:242883
TITLE: Epothilone B stabilizes microtubili of macrophages like taxol without showing taxol-like endotoxin activity
AUTHOR(S): Muhlradt, Peter F.; Sasse, Florenz
CORPORATE SOURCE: Gesellschaft fur Biotechnologische Forschung mbH, Arbeitsgruppe Immunbiologie, Braunschweig, D-38124, Germany
SOURCE: Cancer Research (1997), 57(16), 3344-3346
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Sep 1997
AB Epothilones are a new class of potential antitumor compds. that were isolated from the myxobacterium Sorangium cellulosum. Epothilones have effects on the cytoskeleton similar to those of the antineoplastic drug Taxol. Both compds. inhibit cell proliferation by stabilizing microtubuli, and they compete for

the same binding site. In addition, Taxol displays endotoxin-like properties in that it activates macrophages to synthesize proinflammatory cytokines and nitric oxide. We measured nitric oxide release by IFN-γ-treated murine macrophages as an indicator of macrophage activation by epothilone B. Although epothilone B showed the expected effects on the microtubuli, there was no indication of macrophage stimulatory activity by epothilone B, nor did epothilone B inhibit lipopolysaccharide-mediated nitric oxide release. We conclude that, unlike Taxol, epothilone-mediated microtubuli stabilization does not trigger endotoxin-signaling pathways. Moreover, because the endotoxin-like activity of Taxol may be the cause of some nonhematol. clin. side effects, it is to be expected that such effects may not occur with epothilones.

CC 1-6 (Pharmacology)

ST microtubule epothilone B antitumor endotoxin signaling

IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endotoxins; epothilone B stabilizes microtubili of macrophages like taxol without showing taxol-like endotoxin activity in relation to antitumor activity)

IT Microtubule
(epothilone B stabilizes microtubili of macrophages like taxol without showing taxol-like endotoxin activity in relation to antitumor activity)

IT 152044-54-7, Epothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epothilone B stabilizes microtubili of macrophages like taxol without showing taxol-like endotoxin activity in relation to antitumor activity)

IT 10102-43-9, Nitric oxide, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(lipopolysaccharide-mediated release; epothilone B stabilizes microtubili of macrophages like taxol without showing taxol-like endotoxin activity in relation to antitumor activity)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:359321 CAPLUS Full-text
DOCUMENT NUMBER: 127:92475
TITLE: Isolation, structure elucidation, and synthesis of a macrophage stimulatory lipopeptide from Mycoplasma fermentans acting at picomolar concentration
AUTHOR(S): Muhlradt, Peter F.; Kiess, Michael; Meyer, Holger; Sussmuth, Roderich; Jung, Gunther
CORPORATE SOURCE: Immunobiology and Structure Research Groups, Gesellschaft fur Biotechnologische Forschung mbH, Braunschweig, D-38124, Germany
SOURCE: Journal of Experimental Medicine (1997), 185(11), 1951-1958
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Jun 1997

AB Macrophages are typically stimulated by components of microbial cell walls. Surprisingly, cell wall-less mycoplasmas can also very efficiently stimulate macrophages. We showed recently that mycoplasma-derived lipopeptides constitute the active principle. We have now isolated a clone of Mycoplasma fermentans expressing mainly one macrophage- stimulating lipopeptide. This lipopeptide was detergent-extracted and isolated by reversed-phase high-performance liquid chromatog., using nitric oxide release from C3H/HeJ mouse macrophages as bioassay for detection. In contrast to "conventional" bacterial lipoproteins, this lipopeptide had a free NH2 terminus. Amino acid composition, sequence, and the mol. weight of 2163.3 are consistent with the following structure: S-(2,3- bisacyloxypropyl)cysteine-GNNDESNISFKEK with one mole C16:0, and a further mode of a mixture of C18:0 and C18:1 fatty acid per lipopeptide mol. The sequence could not be found in either the protein identification resource nor the Swiss Prot data bank. We named this 2-kd lipopeptide, macrophage-activating lipopeptide-2 (MALP-2). Synthetic dipalmitoyl MALP-2 and mycoplasma-derived MALP-2 were compared with the bioassay. Both lipopeptides showed an identical dose dependency with a half-maximal response at 10-11 M concentration MALP-2 may be one of the most potent natural macrophage stimulators besides endotoxin.

CC 10-1 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 15

ST Mycoplasma macrophage stimulatory lipopeptide

IT Mycoplasma fermentans
(isolation, structure elucidation, and synthesis of macrophage stimulatory lipopeptide from Mycoplasma fermentans acting at picomolar concentration)

IT Cytokines
RL: PRP (Properties)
(macrophage-activating factor, MALP-2 (macrophage -activating lipopeptide 2); isolation, structure elucidation, and synthesis of macrophage stimulatory lipopeptide from Mycoplasma fermentans acting at picomolar concentration)

IT Lipopeptides
RL: PRP (Properties)
(macrophage-activating; isolation, structure elucidation, and synthesis of macrophage stimulatory lipopeptide from Mycoplasma fermentans acting at picomolar concentration)

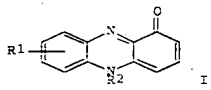
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:221714 CAPLUS Full-text
DOCUMENT NUMBER: 108:221714
TITLE: Preparation of 7- and 8-(carboxyalkyl)pyocyanine derivatives as intermediates for polymer-bound antitumor agents
INVENTOR(S): Morr, Michael; Kakoschke, Christel; Tsai, Hsin; Getzlaff, Rita
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3627310	A1	19880218	DE 1986-3627310	19860812

EP 257333	A1	19880302	EP 1987-111014	19870729
R: CH, DE, FR, GB, LI, NL, SE				
US 4845222	A	19890704	US 1987-79088	19870729

PRIORITY APPLN. INFO.: DE 1986-3627310 A 19860812
OTHER SOURCE(S): CASREACT 108:221714; MARPAT 108:221714
ED Entered STN: 24 Jun 1988
GI



I

AB The title compds. (I; R1 = 7- or 8-alkoxycarbonylalkyl, carboxyalkyl, succinimidoxycarbonylalkyl; R2 = H, alkyl) were prepared as intermediates for oligomer- or polymer-bound antitumor agents. Me 4'-(3,4-diaminophenyl)butyrate and 3-methoxy-o-quinone were stirred 5 h in HOAc/C6H6 to give Me 4'-(1-methoxyphenazinyl)butyrate as a mixture of the 7- and 8-substituted isomers, which were demethylated with AlBr3 in C6H6, saponified with aqueous KOH, esterified with N-hydroxysuccinimide/dicyclohexyldii mide, and N-methylated with Me2SO4 to give I (R1 = 7- and 8-succinimidoxypropyl, R2 = Me).

IC ICM C07D241-46
ICS C07D403-12; A61K031-50

ICI C07D241-46, C07D207-46, C07D207-40; C07D241-46, A61K045-05; C07D241-46, A61K031-50

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 114076-18-5P 114076-19-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for polymer-bound antitumor agents)

L34 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:574133 CAPLUS Full-text
DOCUMENT NUMBER: 144:40486
TITLE: Nitric oxide-generating hydrogels inhibit neointima formation
AUTHOR(S): Masters, Kristyn S. Bohl; Lipke, Elizabeth A.; Rice, Elizabeth E. H.; Liel, Meghan S.; Myler, Heather A.; Zygourakis, Corinna; Tulis, David A.; West, Jennifer L.
CORPORATE SOURCE: Department of Chemical Engineering, Rice University, Houston, TX, USA
SOURCE: Journal of Biomaterials Science, Polymer Edition (2005), 16(5), 659-672
CODEN: JBSEEA; ISSN: 0920-5063
PUBLISHER: VSP
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Jul 2005

AB This study evaluated the effects of localized delivery of nitric oxide (NO) from hydrogels covalently modified with S-nitrosocysteine (Cys-NO) on neointima formation, a key component of restenosis, in a rat balloon-injury model. Soluble Cys-NO was used in preliminary studies to identify dosage ranges that were able to simultaneously inhibit smooth muscle cell proliferation, enhance endothelial cell proliferation, and reduce platelet adhesion. Photo-cross-linked PEG-based hydrogels were formed with covalently immobilized Cys-NO. These materials release NO for approx. 24 h and can be applied to tissues and photo-cross-linked in situ to form local drug-delivery systems. Localized delivery of NO from hydrogels containing Cys-NO inhibited neointima formation in a rat balloon-injury model by approx. 75% at 14 days.

CC 63-5 (Pharmaceuticals)

IT 52-90-4D, L-Cysteine, reaction product with PEG derivs. and nitric oxide 400754-58-7D, reaction product with L-cysteine
RL: RCT (Reactant); RACT (Reactant or reagent)
(nitric oxide-generating hydrogels inhibit neointima formation)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1130042 CAPLUS Full-text
DOCUMENT NUMBER: 142:435694
TITLE: Improved hemocompatibility of poly(ethylene terephthalate) modified with various thiol-containing groups
AUTHOR(S): Gappa-Fahlenkamp, Heather; Lewis, Randy S.
CORPORATE SOURCE: School of Chemical Engineering, Oklahoma State University, Stillwater, OK, 74078, USA
SOURCE: Biomaterials (2005), 26(17), 3479-3485
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 27 Dec 2004

AB Thiol groups were attached to polyethylene terephthalate (PET) to promote the transfer of a known platelet inhibitor, nitric oxide (NO), from nitrosated thiols naturally found in the body to PET, followed by the release of NO from PET to prevent platelet adhesion. In order to immobilize the most thiols on the modified polymer, the processing parameters used to attach the following three thiol containing groups were assessed: L-cysteine, 2-iminothiolane, and a cysteine polypeptide. When comparing the immobilized concns. of thiol groups from each of the optimized processes the amount of immobilized thiol groups increased in order with the following groups: cysteine polypeptide <2-iminothiolane <L-cysteine. The effect of each optimized polymer on platelet adhesion was studied by in vitro expts. utilizing a parallel plate perfusion chamber. Platelets in the following solns. were tested: Tyrode's buffer, 7 μM nitrosated bovine serum albumin in Tyrode's buffer, 50% plasma in Tyrode's buffer, and 50% whole blood in Tyrode's buffer. All of the polymers demonstrated a significant decrease in platelet adhesion compared to controls when exposed to the BSANO, plasma and whole blood solns. The most significant decrease was for the L-cysteine modified polymer in the plasma solution with a 65% decrease.

CC 63-7 (Pharmaceuticals)

IT 52-90-4DP, L-Cysteine, 4reaction products with polyethylene terephthalate 107-15-3DP, Ethylenediamine, reaction products with polyethylene terephthalate 111-30-8DP, Glutaraldehyde, reaction products with polyethylene terephthalate 6539-14-6DP, 2-Iminothiolane, reaction products with polyethylene terephthalate 7093-67-6DP, Pentaglycine, reaction products with polyethylene terephthalate 25038-59-9DP, cysteine derivs. modified 850920-26-2DP,

reaction products with polyethylene terephthalate
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(improved hemocompatibility of poly(ethylene terephthalate) modified with various thiol-containing groups)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:996214 CAPLUS Full-text
DOCUMENT NUMBER: 141:427979
TITLE: Stabilisation of unglycosidated interferon-γ manufactured in bacteria by modification with polyethylene glycol
INVENTOR(S): Brunner, Herwig; Zakaria, Hayssam; Otto, Bernd; Thomas, Tobias; Battermann, Florian; Kresin, Marco; Busche, Andreas; Schmalz, Christian
PATENT ASSIGNEE(S): Fraunhofer-Gesellschaft Zur Foerderung Der Angewandten Forschung E.V., Germany
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099245	A1	20041118	WO 2004-EP4677	20040503

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2003-10320223 A 20030505
ED Entered STN: 19 Nov 2004

AB A method stabilizing unglycosidated interferon-γ manufactured in a prokaryotic host to improve its serum half-life is described. The method involves conjugating the protein with polyethylene glycol via thiol or amino side groups. Amino acid cysteine, asparagine, glutamine, lysine, arginine, and/or histidine are particularly suitable for said type of modification. The protein may be modified by the substitution of amino acids to form sites for conjugation.

IC ICM C07K014-57
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 15

IT 52-90-4D, L-Cysteine, interferon γ containing, conjugates with polyethylene glycol, biological studies 56-85-9D, L-Glutamine, interferon γ containing, conjugates with polyethylene glycol 56-87-1D, L-Lysine, interferon γ containing, conjugates with polyethylene glycol, biological studies 70-47-3D, L-Asparagine, interferon γ containing, conjugates with polyethylene glycol, biological studies 71-00-1D,

L-Histidine, interferon γ containing, conjugates with polyethylene glycol, biological studies 74-79-3D, L-Arginine, interferon γ containing, conjugates with polyethylene glycol, biological studies 25322-68-3D, Polyethylene glycol, conjugates with interferon-γ
RL: BUU (Biological use, unclassified); MOA (Modifier or additive use); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(stabilization of unglycosidated interferon-γ manufactured in bacteria by modification with polyethylene glycol)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:489100 CAPLUS Full-text
DOCUMENT NUMBER: 142:204368
TITLE: Development and in vivo evaluation of an oral insulin-PEG delivery system
AUTHOR(S): Calceti, P.; Salmaso, S.; Walker, G.; Bernkop-Schnurch, A.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Padua, Padua, 35131, Italy
SOURCE: European Journal of Pharmaceutical Sciences (2004), 22(4), 315-323
CODEN: EPSCED; ISSN: 0928-0987
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 17 Jun 2004
AB Insulin-monomethoxypoly(ethylene glycol) derivs. were obtained by preparation of mono- and di-terbutyl carbonate insulin derivs., reaction of available protein amino groups with activated 750 Da PEG and, finally, amino group de-protection. This procedure allowed for obtaining high yield of insulin-1PEG and insulin-2PEG. In vivo studies carried out by s.c. injection into diabetic mice demonstrated that the two bioconjugates maintained the native biol. activity. In vitro, PEGylation was found to enhance the hormone stability towards proteases. After 1 h incubation with elastase, native insulin, insulin-1PEG and insulin-2PEG undergo about 70, 30 and 10% degradation, resp., while in the presence of pepsin protein degradation was 100, 70 and 50%, resp. The attachment of low mol. weight PEG did not significantly (P>0.05) alter insulin permeation behavior across the intestinal mucosa. Insulin-1PEG was formulated into mucoadhesive tablets constituted by the thiolated polymer poly(acrylic acid)-cysteine. The therapeutic agent was sustained released from these tablets within 5 h. In vivo, by oral administration to diabetic mice, the glucose levels were found to decrease of about 40% since the third hour from administration and the biol. activity was maintained up to 30 h. According to these results, the combination of PEGylated insulin with a thiolated polymer used as drug carrier matrix might be a promising strategy for oral insulin administration.
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 34, 35
IT 52-90-4D, L-Cysteine, reaction products with poly(acrylic acid) 9003-01-4D, Poly(acrylic acid), reaction products with L-cysteine
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and activity of insulin-PEG conjugate delivered in tablet form)

L34 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:399614 CAPLUS Full-text
DOCUMENT NUMBER: 141:355142

TITLE: A Novel strategy to modify adenovirus tropism and enhance transgene delivery to activated vascular endothelial cells in vitro and in vivo
AUTHOR(S): Ogawara, Ken-ichi; Rots, Marianne G.; Kok, Robbert J.; Moorlag, Henk E.; van Loenen, Anne-Miek; Meijer, Dirk K. F.; Haisma, Hidde J.; Molema, Grietje
CORPORATE SOURCE: Medical Biology Section, Department of Pharmacokinetics and Drug Delivery, Groningen University Institute for Drug Exploration, Groningen, Neth.
SOURCE: Human Gene Therapy (2004), 15(5), 433-443
CODEN: HGTHE3; ISSN: 1043-0342
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 17 May 2004
AB To assess the possibilities of retargeting adenovirus to activated endothelial cells, we conjugated bifunctional polyethylene glycol (PEG) onto the adenoviral capsid to inhibit the interaction between viral knob and coxsackie-adenovirus receptor (CAR). Subsequently, we introduced an αv integrin-specific RGD peptide or E-selectin-specific antibody to the other functional group of the PEG mol. for the retargeting of the adenovirus to activated endothelial cells. In vitro studies showed that this approach resulted in the elimination of transgene transfer into CAR-pos. cells, while at the same time specific transgene transfer to activated endothelial cells was achieved. PEGylated, retargeted adenovirus showed longer persistence in the blood circulation with area under plasma concentration-time curve (AUC) values increasing 12-fold compared to unmodified virus. Anti-E-selectin antibody-PEG-adenovirus selectively homed to inflamed skin in mice with a delayed-type hypersensitivity (DTH) inflammation, resulting in local expression of the reporter transgene luciferase. This is the first study showing the benefits of PEGylation on adenovirus behavior upon systemic administration. The approach described here can form the basis for further development of adenoviral gene therapy vectors with improved pharmacokinetics and increased efficiency and specificity of therapeutic gene transfer into endothelial cells in disease.
CC 63-6 (Pharmaceuticals)
IT 52-90-4DP, Cysteine, reaction products with PEG functionalized adenovirus 76931-93-6DP, N-Succinimidyl S-acetyl thioacetate, reaction products with antibodies and PEG functionalized adenovirus 174459-58-6DP, reaction products with adenoviral capsid amino groups and peptides or antibodies 393781-65-2DP, conjugates to human anti-mouse antibody and PEG functionalized adenovirus 393781-66-3DP, reaction products with PEG functionalized adenovirus
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(modification of adenovirus tropism with functionalized PEG and peptides and antibody for enhanced transgene delivery to activated vascular endothelial cells in vitro and in vivo)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:163911 CAPLUS Full-text
DOCUMENT NUMBER: 124:194348
TITLE: PEGylation reagents and biologically active compounds formed therewith
INVENTOR(S): Kohno, Tadahiko; Kachensky, Dave; Harris, Milton
PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9534326	A1	19951221	WO 1995-US7555	19950614
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6552170	B1	20030422	US 1994-259413	19940614
AU 9528286	A	19960105	AU 1995-28286	19950614
EP 758906	A1	19970226	EP 1995-923865	19950614
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9507999	A	19970812	BR 1995-7999	19950614
FI 9604985	A	19961216	FI 1996-4985	19961212
NO 9605342	A	19970214	NO 1996-5342	19961212
PRIORITY APPLN. INFO.:			US 1994-259413 A	19940614
			US 1990-506522 A2	19900406
			US 1990-555274 B2	19900719
			US 1991-669862 B2	19910315
			US 1992-850675 B2	19920313
			WO 1995-US7555 W	19950614

ED Entered STN: 21 Mar 1996
AB Biol. active conjugates are disclosed which are formed by reaction of a thiol moiety of a biol. active mol. with a non-peptidic polymer having an active sulfone moiety. Also disclosed are compds. having the formula R1-R2 wherein at least one of R1 and R2 is a biol. active mol. having a reactive thiol moiety which forms a covalent bond with X, a Michael acceptor-activated non-peptidic polymer. Further disclosed are methods of making the conjugates and compds. of the present invention as well as pharmaceutical compns. containing them. In addition, activated polymers suitable for attachment to a variety of mols. and surfaces are disclosed. Among the reagents synthesized is e.g. a vinyl sulfone NHS-ester heterobifunctional PEG(3400) reagent. Also described are preparation of conjugates of PEG reagents with IL-1ra (interleukin-1 receptor antagonist) and with TNF binding protein c105 mutein. A TNFbp c105 dumbell (prepared with PEG-bis-vinyl sulfone) inhibited exptl. allergic encephalomyelitis, reduced central nervous system inflammation, and protected against endotoxin lethality.
IC ICM A61K047-48
CC 1-12 (Pharmacology)
Section cross-reference(s): 35, 63
IT 52-90-4DP, L-Cysteine, albumin conjugates 174459-58-6P
174459-59-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(PEG derivative preparation, conjugation with biol. active mols., and therapeutic activity)

L34 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:175808 CAPLUS Full-text
DOCUMENT NUMBER: 118:175808
TITLE: Drug-containing protein-bonded liposome
INVENTOR(S): Tagawa, Toshiaki; Hosokawa, Saiko; Nagaike, Kazuhiro

PATENT ASSIGNEE(S): Mitsubishi Kasei Corp., Japan
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 526700	A2	19930210	EP 1992-108527	19920520
EP 526700	A3	19940126		
EP 526700	B1	19980826		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
JP 04346918	A	19921202	JP 1991-118762	19910523
JP 3220180	B2	20011022		
AT 170083	T	19980915	AT 1992-108527	19920520
ES 2120972	T3	19981116	ES 1992-108527	19920520
CA 2069244	A1	19921124	CA 1992-2069244	19920522
CA 2069244	C	20021001		
US 5264221	A	19931123	US 1992-886846	19920522
JP 06184195	A	19940705	JP 1993-195766	19930806
PRIORITY APPLN. INFO.:			JP 1991-118762 A	19910523
			EP 1992-108527 A	19920808

ED Entered STN: 01 May 1993
AB A drug-containing liposome comprises a maleimide residue on its surface, a protein, and a polyalkylene glycol-containing compound, bonded via thiol groups to the maleimide residues. The liposomes are designed to concentrate the drug, especially an antitumor agent at a required site utilizing a specific reactivity of an antibody. Thus, 6-carboxyfluorescein was added to a lipid mixture of dipalmitoylphosphatidylcholine, cholesterol, and maleimide-modified dipalmitoyl phosphatidylethanolamine to give a maleimide-containing fluorescent dye-loaded liposome. To the liposome, antitumor monoclonal antibody Fab' and thiol-modified polyethylene glycol were added to obtain an antibody-bonded PEG-modified liposome. The obtained liposome was highly reactive with human cancer cell line MKN 45.
IC ICM A61K047-48
ICS A61K009-127
CC 63-6 (Pharmaceuticals)
IT 52-90-4D, Cysteine, reaction products with bis(polyethylene glycol) chlorotriazine 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies 2644-64-6, Dipalmitoylphosphatidylcholine 3301-79-9, 6-Carboxyfluorescein 5681-36-7D, Dipalmitoyl phosphatidylethanolamine, reaction products with (maleimidocaproyloxy)succinimide 23214-92-8, Adriamycin 55750-63-5D, reaction products with dipalmitoyl phosphatidylethanolamine 146419-86-5D, reaction products with cysteine
RL: BIOL (Biological study)
(antibody-bonded antitumor liposomes containing)

L34 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:192789 CAPLUS Full-text
DOCUMENT NUMBER: 108:192789
TITLE: Topical therapeutic composition containing lymphokines, with polymer bound redox couples as an oxidation inhibitor system
INVENTOR(S): Evans, Sean A.; Terpinski, Eva A.; Testa, Douglas
PATENT ASSIGNEE(S): Interferon Sciences, Inc., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM

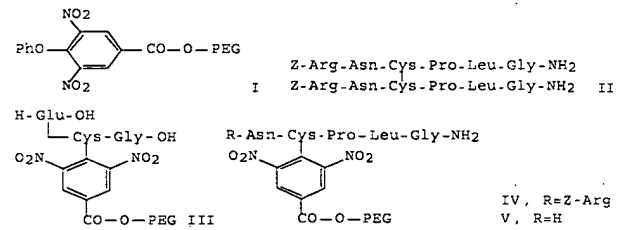
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4710376	A	19871201	US 1985-697320	19850201
CA 1289883	C	19911001	CA 1986-502248	19860219
IL 77975	A	19900610	IL 1986-77975	19860224

PRIORITY APPLN. INFO.: US 1985-697320 19850201
ED Entered STN: 28 May 1988
AB A substantially nontoxic, stable topical therapeutic composition contains (a) a therapeutically active component which is susceptible to oxidative degradation; (b) an oxidative degradation-inhibitory amount of a redox system containing (1) a water soluble polymer with many covalently bound reducing groups and (2) a water soluble polymer with many covalently bound oxidizing groups, and (c) an aqueous vehicle base compatible with the therapeutically active component. Hydroxyethyl cellulose was treated with cysteine-HCl to give hydroxyethyl cellulose-bound cysteine-HCl (I); hydroxyethyl cellulose was treated with cystine-HCl to give hydroxyethyl cellulose-bound cystine-HCl (II). Interferon ointment (100 g) contained (a) hydroxyethyl cellulose 2.5, glycerin 10.0, I (1% cysteine bound) 1.5, and II (1% cystine bound) 1.5 g, water 60.8 mL; (b) propylparaben 0.06, methylparaben 0.25, and glycerin 10 g; and (c) concentrated sterile interferon stock solution 13 mL, soybean trypsin inhibitor (50 mg/mL) 0.52 mL. Mixts. (a) and (b) were combined to form a gel and cooled to 4°, and (c) was added; after mixing the composition was loaded into sterile Al ointment tubes which were crimped closed.
IC ICM A61K031-745
ICS A61K045-02
INCL 424083000
CC 63-6 (Pharmaceuticals)
IT 52-89-1DP, Cysteine hydrochloride, esters with hydroxyethyl cellulose 52-90-4DP, Cysteine, esters with hydroxyethyl cellulose or polyethylene glycol 56-89-3DP, Cystine, esters with hydroxyethyl cellulose or polyethylene glycol 107-96-0DP, Mercaptopropionic acid, esters with hydroxyethyl cellulose or polyethylene glycol 1002-18-2DP, esters with hydroxyethyl cellulose or polyethylene glycol 1119-62-6DP, esters with hydroxyethyl cellulose or polyethylene glycol 9004-62-0DP, Hydroxyethyl cellulose, reaction products with mercapto-containing reducing and dithio-containing oxidizing compds. 25322-68-3DP, Polyethylene glycol, reaction products with mercapto-containing reducing and dithio-containing oxidizing compds.
RL: PREP (Preparation)
(preparation of, as stabilizer for lymphokine formulations)

L34 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:457478 CAPLUS Full-text
DOCUMENT NUMBER: 91:57478
TITLE: 4-Phenoxy-3,5-dinitrobenzoylpolyethyleneglycol: reversible attachment of cysteine-containing polypeptides to polymers in aqueous solutions
AUTHOR(S): Glass, John D.; Silver, Lester; Sondheimer, James; Pande, Chandra S.; Coderre, Jeffrey
CORPORATE SOURCE: Dep. Physiol. Biophys., Mt. Sinai Sch. Med., New York, NY, USA
SOURCE: Biopolymers (1979), 18(2), 383-92
CODEN: BIPMAA; ISSN: 0006-3525
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 12 May 1984
GI



AB Polyethyleneglycol (PEG) (mol. weight 6000) was esterified with 4-phenoxy-3,5-dinitrobenzoyl chloride to give ester I, which reacted rapidly with SH groups of cysteine peptides in aqueous buffers (pH 7) to give a peptide-polymer thio compound linked by a dinitrophenylene bridge. I reacted very slowly with other functional groups of peptides; consequently, I can be selective for SH groups. Reduced glutathione and cystine peptide II (Z = PhCH2O2C) were treated with I to give peptide-polymer thio compds. III and IV, resp. IV underwent trypsin cleavage to give V; consequently, the PEG support does not restrict access of enzymes to peptide bonds. Bovine insulin B chain was also treated with I to give the appropriate peptide-polymer thio-linked compound
CC 34-3 (Synthesis of Amino Acids, Peptides, and Proteins)
IT 52-90-4D, peptides containing
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phenoxydinitrobenzoyl polyethylene glycol, mercapto-bound polyethylene glycol derivative from)

=>